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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

IX. LEPROSY.

General.

In the *Revista Brasileira de Leprologia* (p. 451) is an account of the classification of leprosy, in which many suggestions were made by different workers. These cannot be set out in detail here, and no agreed conclusions were reached. ARNOLD and TILDEN (p. 452) suggest a classification into two forms only, lepromatous and tuberculoid, the latter including the so-called "neural" forms. COCHRANE (p. 1146) gives his opinion that tuberculoid lesions do not become lepromatous.

Epidemiology.

BLOSS (p. 656) reports on leprosy in the southern Sudan where, in 1935, it was estimated that 7 per cent. of the population were affected. A large settlement has been in existence for many years, and has been useful for the segregation of infective patients in special camps. Chaulmoogra has proved valuable. The diminishing numbers found in recent years, and the fact that the proportion of patients below the age of 20 is diminishing, suggest that the disease is being brought under control.

In a leprosy survey of part of the Belgian Congo, DEGOTTE (p. 340) found incidence rates varying from 2 to 6 per cent.; the highest incidence was in persons aged 30–40. Most of the lepromatous cases are now segregated in this area. RADNA (p. 1146) brings evidence to show that leprosy has increased very considerably in recent years in the north-east of the Belgian Congo, where the incidence is now some 3·4 per cent., though two generations ago it was probably not much more than 0·6.

DHARMENDRA (p. 452) shows that the humid province of Bengal has a high leprosy rate, up to 3 per cent., and estimates the number of cases at 200,000–300,000. For these there are only 7 indoor institutions, with 786 beds, and 150 out-patient clinics. Isolation of infective patients, therefore, is not nearly adequate.

SHLIMOVITZ (p. 750) has found a few cases of leprosy, obviously old-standing, in the mountainous interior of New Guinea, where the disease had not previously been seen, though well known on the coast.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

IBARRA PÉREZ and GONZÁLEZ PRENDES (p. 563) give an account of leprosy in Cuba, where the known incidence is 0·53 per 1,000, and the probable incidence considerably higher. The same authors (p. 933) have written of the incidence of leprosy in Cuba, according to race. They make the point that any differences in racial incidence are due rather to economic causes than to racial susceptibility.

An enquiry held in the Philippines by DOULL *et al.* (p. 453) indicates that the risk of acquiring lepromatous leprosy is highest for persons exposed to infection before the age of 5 years, and decreases progressively as the age at time of exposure increases. This is true for both males and females, but there is also strong evidence that males at all ages are more susceptible than females to leprosy. The average interval between exposure to infection below the age of 10 and recognition of disease was 10·5 years, but for those first exposed after the age of 10 it was only 6 years. BANCROFT *et al.* (p. 454) show that in the Philippines the risk of infection of persons living in a house with a lepromatous patient is 8 times as great as that of those not known to have had such household contact. The risk of infection from a neural case is apparently no greater than among the general population.

TRESPALACIOS and GONZÁLEZ PRENDES (p. 934) have traced the earliest symptoms, and calculated the probable age at infection, of 315 patients in Havana. In 63 per cent. the symptoms appeared first before the age of 25, and the average was 23 years, with probable first infection some 5 years earlier. Most of these patients had lepromatous disease.

CANAAN (p. 340) quotes his own long experience of leprosy to emphasize the low degree of infectivity of this disease ; new infections are rare after the age of 30–35.

MOISER (p. 454) contends that cockroaches may play some part in the transmission of leprosy in S. Rhodesia, and gives reasons for his opinion.

Aetiology : Pathology : Clinical Findings.

MONTEL (p. 1152) describes Macchiavello's method of staining leprosy bacilli. In staining the leucocyte layer of citrated blood some of the bacilli are stained, but some are not. He suggests that the latter, presumably lacking a waxy coat, may be the infective forms. He makes the point that blood for examination should be drawn from a vein by puncture where the skin is normal. By staining blood in this way, positive results are usual in lepromatous disease, but never in tuberculoid and nerve cases.

MONTEL *et al.* (p. 454) note that leprosy bacilli are found in large monocytes of the blood, and that these are more numerous in blood taken under pressure from the ear. They are also easily found in the leucocyte layer of centrifuged, citrated, venous blood.

ROW (p. 1147) claims to have cultivated the leprosy bacillus, from a nodule, in haemoglobinized saline to which a culture of *Leishmania* was added, and thereafter on agar and glycerinated potato.

HASSELTINE (p. 457) comments on the frequent presence of acid-fast organisms, which are not leprosy bacilli, in the skin, and states that the most reliable method for demonstrating leprosy bacilli is to scrape a skin incision after the method advocated by Wade, repeated in a second area of skin, and to rely only on finding the typical bundle arrangement. CAMPOS and SOUZA (p. 47) discuss the difficulty in diagnosis sometimes encountered between leprosy and syphilis of the skin. The Wassermann reaction is important if negative, but it may be positive in leprosy. Biopsy with discovery of the organism is decisive.

ARGÜELLO PITT and CONEJOS (p. 849) found leprosy bacilli in the lesions of 8 of 78 patients with tuberculoid leprosy. Six were in the state of reaction, two were not.

TAYLOR (p. 342) has found leprosy bacilli in the wall of the gall bladder, and in the edges of ulcers of the large intestine, in a case of leprosy. The gastro-intestinal and biliary tracts are generally supposed to escape infection.

TILDEN (p. 455) shows that in lepromatous leprosy the reticulo-endothelial system is especially involved. The nodules are predominantly composed of histiocytes, and the globi are large or fused histiocytes. Liver and spleen commonly show minute foci in which the reticulo-endothelial tissues are similarly involved. The lungs are the least affected of the internal organs. In 16 autopsies, tuberculous complications of leprosy were found in 7.

MOM and BASOMBRIO (p. 455) have continued their studies of spreading factor in lepromatous skin, and now show that the diffusion activity of an extract of such skin is inversely proportionate to the number of *Myco. leprae* it contains. Skin from tuberculoid leprosy is about as active as normal skin.

GONZÁLEZ PRENDES and IBARRA PÉREZ (p. 226) have attempted an assessment of the duration of leprosy. The average duration, in 270 cases, was 23 years, with extremes of 3 and 56.

ARNOLD (p. 751) gives a description of the lesions of lepromatous leprosy, and compares them with those of neural leprosy. The prognosis of the two forms is very different. For details the original should be consulted.

PRABHU (p. 653) gives an account of leprosy of the upper air passages. Nasal infections are the result of general, rather than of local, infections; they are rare in simple macular leprosy, but not uncommon in major tuberculoid disease. The course of these lesions is described, and an account is given of leprosy of the mouth, pharynx and larynx; the last may necessitate tracheotomy on account of the oedema which often occurs.

Leprotic laryngitis is found only in lepromatous disease, and commences with great thickening of the epiglottis; spread to the vocal cords produces stenosis which requires operative relief. SLOAN (p. 460) discusses tracheotomy for this condition; it quickly relieves the stenosis, but although many patients continue to wear a tube for years, there is a fairly heavy mortality rate, deaths being due, largely, to the general condition which made the operation necessary.

CERRI (p. 749) examined blood, bone marrow, gland juice and nasal mucus from a series of leprosy patients. Anaemia, almost always hypochromic, was common. Leprosy bacilli were found in the marrow and glands in some of the lepromatous and mixed cases. Details of the findings should be sought in the original.

GRUENFELDER and LASCH (p. 1148) discuss the effect leprosy may have on the sexual organs, and relate these to the effects on the olfactory system. They think that there is some connexion between the two systems, but it is not clear.

HARLEY (p. 1148) describes the lesions of ocular leprosy as he has seen them in 150 cases in Panama, where 90 per cent. of patients show some ocular involvement, and where the only patients free from this are in the early stage of the disease. More than half the cases are of severe involvement, interfering with sight. The disease affects chiefly the anterior segment. Conjunctivitis is common, but the cornea is the most vulnerable part, being involved in 87 of the 150 cases; the lesion was usually superficial keratitis. The iris is also vulnerable, and iritis, or its sequelae, was observed in over half the cases. Fundus changes were not found. Treatment of these conditions was largely confined to palliative measures. CHORINE (p. 564) remarks that various authors have given very different estimates of the incidence of ocular lesions in leprosy, but that most of them agree that the longer the duration the commoner the ocular complications, and that they are more frequent in lepromatous than in neural

leprosy. He uses a mixture of acetamide and sulphanilamide in water, injected round the circumference of the orbit, in the treatment of ocular complications, and claims good results. The injections are painful and a local anaesthetic is necessary. Details of this treatment should be sought in the original. FERNÁNDEZ and SOTO (p. 850) note that the treatment of ocular complications of leprosy is usually unsatisfactory, and give an account of favourable results obtained by the use of intravenous injections, given very slowly, of benzylic esters of chaulmoogra (Neochaulmestrol). As a rule, improvement followed weekly injections of 1·5–2 cc., and the authors think that some of the value may be due to the pyrexia provoked by the drug. This treatment seems to be the most efficacious of all those hitherto employed, for acute ocular complications of leprosy. BLANCO (p. 851) injects alcohol into the ciliary or ophthalmic ganglia for relief of ocular pains in leprosy, after preliminary local anaesthesia. The operation evidently needs great care and skill, but the author quotes 6 cases in which the procedure was successful in relieving pain, photophobia and lachrymation. The lachrymal glands are often infected, and their extirpation removes one focus of infection and, according to AMENDOLA (p. 225), leads to improvement of other ocular lesions, if these are present.

Tests.

In considering a series of lepromin tests of persons not suffering from leprosy, of whom some had and some had not lived in leprosy countries, BECHELLI *et al.* (p. 225) think that the delayed reaction does not necessarily indicate latent infection, but may be the result of allergy to the lepromin injected 3–4 weeks before. The early reaction, also, does not necessarily indicate infection or sensitization to lepromin, but, in the authors' opinion, may be due to sensitization by the tubercle bacillus. CONVIT *et al.* (p. 457) tested tuberculous and other persons with lepromin, in New York, where leprosy is not endemic. A considerable number of positive results were obtained, which indicate that infection with the tubercle bacillus may produce sensitivity to lepromin. HARRELL and HORNE (p. 655) also think that there may be common sensitizing antigens in *Myco. tuberculosis* and *Myco. leprae*, in view of the fact that they found a high incidence of strong lepromin reactions in tuberculous persons. There is no evidence that sarcoid is a form of leprosy, a conclusion also reached by WEEKS and SMITH (p. 654).

In tuberculoid leprosy, SCHUJMAN (p. 1152) found the tuberculin test and the Mitsuda test positive in 96 per cent. of a series of cases, but the latter was negative in nodular leprosy, whereas the tuberculin test, though not so often positive as in tuberculoid disease, was positive in 81 per cent. of lepromatous cases.

DAVEY (p. 1151) discusses the difficult subject of allergy in leprosy ; it is best seen in the tuberculoid form. The early lepromin reaction and the tuberculoid response are distinct, but related, indications of the allergic state. This paper should be read in the original.

In a test of the leprolins of de Souza-Araujo, and of ordinary lepromin, PEREIRA (p. 564) found that the results were not in accord in a series of patients.

CHORINE (p. 341) has devised a new flocculation reaction for leprosy, which is based upon the Rubino reaction, and in which an antigen from formolized red cells is used with the serum of the suspected patient, and flocculation is measured. High degrees of reaction are found in lepromatous leprosy and during the lepra reaction ; the test has both diagnostic and prognostic value.

OLMOS CASTRO and BONATTI (p. 849) describe the preparation of an antigen from lepromatous tissue, which flocculates with a proportion of sera from lepromatous cases, and occasionally from tuberculoid cases. The results closely approximate to those with the Kahn and certain other reactions ; the

test is not satisfactory for diagnosis. The same authors (p. 850) found that complement in sera of leprosy patients was within normal limits.

DUEÑAS and ABAD (p. 935) quote results of several tests (including the Rubino test) in leprosy. They remark that when the results for leprosy tests, and tests for syphilis, are both positive, there is probably a dual infection of leprosy and syphilis.

Treatment.

MUIR (p. 654) draws a comparison between lepromatous leprosy and filarial elephantiasis as regards septic infection and the development of pachydermatous conditions, in both cases associated with lymphatic obstruction and periodic inflammatory changes. Sepsis, and possibly allergic reactions, may be the cause of lepra reactions, which may be controlled by promin or diasone. These, and penicillin, probably act by their effect on septic infection.

FAGET and POGGE (p. 343) report further on the use of promin in leprosy, recording the results so far seen in 137 cases. Routine treatment consists of 3 to 5 gm. injected intravenously each day, six days each week, for courses up to 2 weeks, with intervals of one week between courses. The longer the duration of treatment, and the higher the doses (within toxic limits), the better the results ; improvement is recorded in up to 72·5 per cent. of certain categories. Promin is not claimed to be a specific remedy, but it does cause retrogression of some lesions ; further chemotherapeutic research may indicate a more effective drug—perhaps diasone. FITE and GEMAR (p. 751) have given daily intravenous doses of promin, usually of 5 gm., for courses of 3 weeks separated by intervals of 1 week, over periods up to 4 years, with encouraging results. Clinical improvement is slow, but usually steady, and febrile exacerbations are rare. Promin probably acts by eliminating the bacilli from the circulation, and thus preventing spread. The organisms in the tissues gradually decrease in accordance with the self-healing tendency of the disease.

MUIR (p. 458) has treated a series of lepromatous patients with diasone, either injected intravenously or given by mouth. Details of dosage are given in the original abstract. The results are very encouraging, especially in those treated for 3 months or more, and general improvement in health, as well as improvement of local lesions, was noted in the great majority of cases. Anaemia was sometimes provoked, but responded to liver and iron. The results are very similar to those produced by promin.

CHORINE (p. 459) obtained some evidence of benefit from the use of acetamide and of sulphanilamide in rat leprosy, but there was no advantage in giving them together.

LIMA and CERQUEIRA (pp. 47, 226) report very favourably indeed on the treatment of lepromatous leprosy with " Soluthiazamide " given intravenously.

FAGET and POGGE (p. 460) state that penicillin has no curative action on the essential lesions of leprosy ; on the other hand, GUILLEN PRATS and GOMEZ LUCAS (p. 936) give an account of a patient with severe lepromatous disease, who was greatly benefited by a course of penicillin, which, incidentally, caused febrile reactions after the early injections.

PEREIRA (p. 609) has written a book on the treatment of leprosy, as he has given it in Gôa. In general he finds that chaulmoogra gives the most certain results, but that there is a place for Reenstierna's serum, vaccines, venoms, vitamins and other substances for certain types of disease.

GUICHARD (p. 343) describes a simple method of preparation of esters of the fatty acids of *Hydnocarpus anthelmintica* ; details are given in the original abstract.

MONTEL (p. 344) writes favourably of Charpy's method of treatment of lupus (with vitamin D, calcium gluconate and milk), applied to leprosy, but reports only two cases.

The painful neuritis which affects more than half of the ambulatory patients at Carville, and which is due mainly to pressure on nerve trunks produced by lymphocyte infiltration, has been treated, with some success, by administration of vitamin B_1 (orally or by injection), application of heat, and intravenous injection of calcium gluconate (POGGE, p. 456).

LENGAUER (p. 459) writes of the beneficial effect of palm oil, locally on chronic ulcers, and by the mouth, in leprosy.

GUADAGNINI (p. 851) has had some success in treating leprous ulcers of nervous origin by intra-arterial injections of 2 per cent. novocaine into the femoral artery twice or thrice each week.

FENNEL (p. 458) quotes two cases in which removal of initial skin lesions by surgical means was apparently entirely successful. In comment, ROGERS makes the point that such successful excisions support the modern view that leprosy infection usually occurs through the entry of the causative organisms through skin abrasions or punctures, including punctures of insect bites.

TROUT (p. 341) describes antigens and vaccines prepared from an acid-fast organism. He has used these both in treatment and in prophylaxis.

Writing from a leprosy hospital in India, DOW (p. 460) points out that few, if any, leprosy patients are mentally healthy; he stresses the advantages of, and need for, occupational therapy.

SCHUJMAN (p. 846) discusses the criteria for the release of leprosy patients from hospital, quoting the practices of various well-known institutions, and finally giving certain guides of his own. These should be sought in the original abstract; they vary according to type of disease and period of freedom from infectivity. CERBONI *et al.* (p. 847) discuss the same subject, giving details of the examinations which should be carried out at the various stages, and the progressive steps to be taken towards conditional discharge (with continued observation) and definitive discharge. Details should be sought in the original abstract. FIOL (p. 848) suggests that even definitive discharge should not be absolute, but should be subject to annual revision. GARZÓN and ARGÜELLO PITT (p. 849) discuss the whole subject of discharge.

CHANDY (p. 656) stresses the difficulties which face discharged patients in attempting to obtain employment, or to return to their own villages, in India. He suggests that agricultural and industrial settlements should be created to absorb such persons; these might eventually become self-supporting.

Control.

In the *Leprosy Review* (p. 461) there is a discussion, by various workers, of the question of the best methods for protecting infants born to parents suffering from leprosy. The authors agreed that segregation of infants from parents with infective lesions should be carried out if possible (in India relatives can usually be found who will take care of such children). Preventoria are possible in wealthy countries, but crèches are difficult to organize efficiently in many tropical countries. The point is made that "closed" cases are not dangerous even to infants at the breast.

In a paper read before the Royal Society of Arts, ROGERS (p. 1153) has traced the progress made in leprosy control in the British Empire during the last 30 years. This includes drug treatment, epidemiological studies, provision of agricultural leprosaria and segregation which is rather voluntary than compulsory. The address should be read in full.

Rat Leprosy.

FIELDING (p. 1147), holding that infection in rat leprosy is largely the result of excretion of the organisms in urine and faeces, examined the faeces of a number of leprosy patients and found numerous acid-fast organisms. He has inoculated

rats with such faeces, dried, and subsequently has found acid-fast bacilli in the rats, both locally and internally. He considers that patients excreting acid-fast bacilli are dangerous carriers. He (p. 1154) has published further work in support of his contention that rats become infected with rat leprosy through contact with soil contaminated by the organisms shed by infected rats in urine and faeces.

PRUDHOMME (p. 657) describes a test to decide the vitality of rat-leprosy bacilli maintained dry, *in vacuo*, at 0°–4°C. for long periods.

Charles Wilcocks.

RABIES.

CECCALDI, J., PAQUIER, P., TRINQUIER, E., PELISSIER, A. & VARGUES, R. Présence en Afrique équatoriale française d'un virus rabique des rues d'origine équine naturellement renforcé. [**A Rabies Street Virus of Naturally High Virulence in a Horse in French Equatorial Africa.**] *Ann. Inst. Pasteur.* 1947, June, v. 73, No. 6, 589–91.

At the end of 1945, the authors, working at the Pasteur Institute in Brazzaville, isolated a street virus from the brain of a horse which died within 12 hours of showing symptoms suggesting rabies. A few Negri bodies were found in sections of the brain, and brain tissue emulsified in glycerin produced, on intracerebral inoculation of rabbits, a virus of short incubation period which behaved like a fixed virus.

On isolation, this virus killed rabbits on the 10th and 15th days. After the first rabbit passage, death took place on the eighth day, after the second, on the seventh day, and after the third, on the sixth. Up to September 1946, 24 successive passages had been maintained. The virus has been transmitted to guineapigs, a dog and to mice. The virus was finally identified by cross-immunity tests with known rabies virus.

The authors therefore classify this virus among the viruses of naturally high virulence (*naturellement renforcés*) ; they suggest that these findings, following their previous records of human rabies in French Equatorial Africa, call for rigorous veterinary control and prophylactic measures.

The high virulence of this strain confirms the opinion given by REMLINGER in 1928, that rabies virus and the disease of rabies behave in the tropics in a manner analogous to that in which they behave in Europe.

H. J. O'D. Burke-Gaffney.

REMLINGER, P. & BAILLY, J. Action de la streptomycine sur le virus rabique. [**Action of Streptomycin on Rabies Virus.**] *Bull. Acad. Nat. Méd.* 1947, v. 131, Nos. 17/18, 327–8.

Having already found that penicillin was without action on rabies virus, the authors describe experiments to test the effect of streptomycin on the virus.

Streptomycin solution was used to emulsify brain tissue from a rabbit containing fixed virus. The mixture was inoculated into dogs, but all of them developed rabies, which indicated that the virus was resistant to streptomycin.

The authors suggest that the dual resistance of rabies virus to streptomycin and to putrefaction might be put to good use in the examination of brain-specimens from biting animals, which so frequently arrive in the laboratory in a bad state of putrefaction. This suggestion is supported by a description of an

experiment in which a badly contaminated specimen was emulsified with a solution of streptomycin and inoculated into cats : the original specimen had been rich in bacterial flora, but became sterile. The cats developed rabies, without any signs of accompanying bacterial infection.

It is noted that in some of these experiments the test animals showed neurotoxic reactions soon after the injection of the streptomycin. The authors describe the methods which they employed in further experiments to avoid these accidents. *H. J. O'D. Burke-Gaffney.*

REMLINGER, P. & BAILLY, J. Action du suc d'Agave sur le virus rabique. [**Action of Agave on Rabies Virus.**] *Arch. Inst. Pasteur d'Algérie.* 1947, June, v. 25, No. 2, 87–8 ; also in *C. R. Acad. Sci.* 1947, Apr. 21, v. 224, No. 16, 1133–4.

Agave contains a proteinase and the authors have studied its action, as a vegetable enzyme, on rabies virus, in analogy with such an action known to be produced on the virus by enzymes of animal origin.

Two species were studied, *Agave americana* var. *foliis variegatis* and *A. attenuata*, Salm. In each case, juice expressed from the leaf parenchyma was cleared and mixed with an equal volume of a 1/50 emulsion of rabbit brain containing fixed virus. Various adjustments of *p*H were tried. After 17 hours in the dark at 15°, the mixtures were inoculated under the dura of rats in the case of *A. americana* (0·1 cc.) and mice in the case of *A. attenuata* (0·2 cc.). The emulsion mixed with equal parts of water was used as a control in each case.

Tables indicate that, between *p*H 6·6 and *p*H 11, juice from both species of Agave destroyed the virus *in vitro*, and all the animals survived. The control animals died of rabies [in the first table, the control mixture is shown as "*suc d'agave + eau*".]

Juice from two aloes and from some commercial papains failed to destroy the virus.

The authors state that these two species of Agave should be added to the long list of organic substances (of animal origin) which can destroy rabies virus *in vitro* : and that results support the argument in favour of a protein nature for rabies virus. *H. J. O'D. Burke-Gaffney.*

RIETZ, J. H. **Rabies in the Fox.** *J. Amer. Vet. Med. Ass.* 1947, Aug., v. 111, No. 845, 138–9.

The author examined the brains of 14 foxes in northern West Virginia in connexion with an outbreak of rabies among these animals. Negri bodies were found in 10 of them : in the 4 negative cases, the animals may have been killed too soon for Negri bodies to form. Brief clinical notes are given of each case, from which it is clear that, in contrast with the normally retiring disposition of the fox in the presence of human beings and dogs, these animals were fearless and aggressive and attacked with an abnormally marked show of bravery.

The author notes that a number of those persons reporting the attacks had observed that the foxes were " just too brave to be normal " ; and he points out that, in his own experience, the outstanding and constant symptom of rabies in domestic and wild animals has been this change in behaviour and disposition. Any fox showing a marked change from its normal behaviour should be considered a rabies suspect, especially where the disease is enzoötic.

H. J. O'D. Burke-Gaffney.

HABEL, K. **Ultraviolet Irradiation in the Production of Potent Antirabies Vaccines.** *Pub. Health Rep.* Wash. 1947, May 30, v. 62, No. 22, 791–800. [11 refs.]

The author has made a rabies vaccine by the method of Oppenheimer and Levinson [see this *Bulletin*, 1944, v. 41, 914]. This consists of passing a suspension of virus-containing tissue in a thin film in front of an ultra-violet lamp with a high percentage of emission below 2,000 Å. Mouse and rabbit brain emulsions in concentrations of 5 to 20 per cent. were run through the apparatus and given the minimum exposure to ultra-violet light necessary to produce complete inactivation (0·7 second). Vaccine produced by this method protected mice against 340,000 MLD of active virus, whereas phenolized vaccines protected against a maximum of 13,000 MLD only. The potency of the irradiated vaccine was equally high when made from the concentrated brain suspension. Potency was largely lost after storage for 6 months at 4°C., but was retained in the presence of 0·5 per cent. phenol or chloroform. Some slight protection was also conferred upon guineapigs which had received active virus before the beginning of vaccination.

A similar technique of radiation was carried out with an ordinary low-pressure resonance lamp in place of the special Oppenheimer lamp. Vaccines prepared thus were equally potent, showing that the essential feature of Oppenheimer's method lies in irradiating the material in a thin film, and not in using a lamp with emission below 2,000 Å. *D. J. Bauer.*

MALARIA.

WENGER, R. Das vermehrte Auftreten autochthoner Malaria in Wien. [**Increase of Indigenous Malaria in Vienna.**] *Wien. klin. Woch.* 1947, Feb. 21, v. 59, No. 7, 106–8. [12 refs.]

Malaria among persons, especially the older women, who have not been beyond the town and its suburbs has shown an increased prevalence of late years. Between 1922 and 1944 the number of cases annually did not exceed ten. In 1945 there were 30; in 1946, 140. Of these last, 83 were autochthonous. The greatest number occurred in the hot months of the second quarter of the year. *A. maculipennis* appears to be the chief vector; possibly also *A. bifurcatus* and *A. nigripes* [presumably *A. plumbeus*]. The causes assigned are returned infected persons, the hot weather and the large number of susceptibles. After the first world war, there was a much greater incidence among the civilian population; in successive years from 1917 to 1923 the figures were 14, 32, 3,717, 321, 85, 7 and one. *H. Harold Scott.*

HERNBERG, C. A. **The Epidemiology in Malaria Tertiana in Finland during the Years 1941–1945.** *Acta Med. Scandinavica.* 1947, v. 127, Nos. 3/4, 342–60, 8 figs. (1 map). [36 refs.]

During 1945 there were some 1,252 cases of primary malaria recorded in Finland, all *P. vivax* infections.

Malaria is no new disease in Finland. Severe epidemics were recorded in the nineteenth and in the beginning of the present century, but during the two decades preceding the second world war malaria was almost completely absent. Malaria reappeared in the Finnish Army during the second war against the U.S.S.R. Russian troops were the source of infection. In 1941 there were 57 cases, about half from the Hangö frontier. During the three following years, military cases numbered 583, 262, and 892. Troops on the Carelian Isthmus

suffered most, but cases also occurred in East Carelia. Soldiers carried infection to the southern parts of the country where there were civilian cases: 75 in 1942, 53 in 1943 and 17 in 1944.

The author obtained detailed information about 868 of the 1,252 cases notified in 1945. Only 12 of them were women. All patients were between the ages of 15 and 53: there were 345 in the 20–25 age group. The cases were scattered all over the country. It was impossible that infection could have been acquired in the patient's home districts; in some areas temperatures were too low for transmission to have taken place. May was the month of maximum incidence. The vast majority of the patients had been in the Carelian Isthmus in the previous autumn and it would seem almost certain that the outbreak was due to infections acquired some nine months previously.

The author found that an early summer epidemic provided fewer cases of prolonged incubation than did an autumn epidemic. He considers that light, or rather deficient light, may be the factor determining prolonged incubation.

The disease was benign; there was no death. *Norman White.*

Wilson, D. Bagster. **Malaria in Madagascar.** *East African Med. J.* 1947, Apr., v. 24, No. 4, 171–6.

Madagascar was occupied by British forces from 1942 to 1945 and during the first landings, a very high incidence of malaria occurred among the troops, 29 per cent. becoming infected. Simple control measures were begun and the rates dropped in successive years, 28 per cent. in 1943, 9 per cent. in 1944, to 3 per cent. in 1945.

A survey of the indigenous population around Diego Suarez revealed a high degree of hyperendemicity. The parasite rate in children between one and five years old was 81 per cent., between six and ten years, 93 per cent. and in adults 40 per cent. The spleen rates were about the same. *P. falciparum* was the dominant species, although *P. malariae*, *P. vivax* and *P. ovale* also occurred. The gametocyte rate at the end of the malaria season was 16 per cent. but this dropped to 3 per cent. at the beginning of the next season. Other parts of the island are less malarious and at Fianarantsoa the parasite rate in 98 children was only 10 per cent.

A. gambiae is distributed throughout Madagascar, but in all the higher country, *A. funestus* is the chief vector. The maximum density was 19 anophelines per hut. In addition to a number of mainland species, two new *Anopheles* were discovered, *A. radama* de Meillon, and a second [*A. fuscicolor* van Someren]. 1,573 mosquitoes were dissected and sporozoites were found in 5·6 per cent. *funestus* and 4·0 per cent. *gambiae.* *P. C. C. Garnham.*

Rao, R. B., Rao, H. R. & Sundaresan, B. **Epidemiology of Malaria in the Tungabhadra Project Area of the Ceded Districts of Madras.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 323–57, 1 map & 3 charts.

The "ceded districts" of the Madras Presidency, Bellary, Anantapur, Cuddapah and Kurnool lie between the States of Mysore and Hyderabad and abut on the Bombay Presidency. Much of the area is covered with black cotton soil which produces good crops, provided that the rainfall is sufficient and well distributed. Rainfall is, however, precarious in this region and drought occurs more frequently than in any other part of Madras. As an assurance against famine, the Tungabhadra Irrigation Project was evolved. The scheme consists of the construction of a dam across the Tungabhadra River. Water from the resultant lake, some 35 square miles in extent, would be used to irrigate some 650 square miles of country, containing 312 villages, in the event of a failure of rains. The survey reported in this paper was carried out

so that malaria control measures might be put in hand before the project was initiated.

Spleen examinations were made in all 312 villages. In only 68 villages was there evidence of endemic malaria, though the whole district was liable to epidemic malaria following seasons of abnormal rainfall. Sixteen species of *Anopheles* were collected as adults, larvae or both. The ubiquitous *A. culicifacies* is considered to be the chief vector ; in certain parts of the area *A. stephensi* plays a part in malaria transmission. *A. culicifacies* is most prevalent in November and December, the malaria season. In the restricted area in which *A. stephensi* transmits the disease, the malaria season is somewhat later. Blood smears of children showed the relative prevalence of parasite species to be, *P. malariae* 39·2, *P. vivax* 30·4, *P. falciparum* 30·4 per cent.

Norman White.

DE BURCA, B. **Malaria in Fort Sandeman.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 359–65, 4 figs. on 2 pls., 1 graph & 1 map.

Fort Sandeman is the chief town of the Zhob District in the north-east of Baluchistan. It lies in the Zhob Valley on an open plain 4,700-feet above sea-level, three to four miles east of the Zhob River. The cantonment contained some 2,000 troops and the attached bazaar had a population of about 3,500. Half a mile distant is the village of Apozai, population 445 ; here is the terminus of the narrow gauge railway from Quetta. Apozai has a floating population ; nomad tribes pass through at different times of the year. The climate is dry ; the average annual rainfall is about 10 inches. A piped water supply comes from the Siliaza Valley, 9 miles away, and water for irrigation, in a partly cement channel, comes from the same source. About 1928, the prevalence of malaria attracted attention ; in September 1932, the malaria admission rate was 191 per thousand. Over-irrigation and neglect of irrigation channels was thought to be responsible.

The systematic capture of mosquitoes in 1940 yielded *A. culicifacies* 10,379, *A. stephensi* 6,804, *A. pulcherrimus* 24, *A. superpictus* 160, *A. turkhudi* 115, *A. dthali* 149, *A. sergenti* 15 and *A. fluviatilis* 13. Of 10,330 *A. culicifacies* and *A. stephensi* caught in May and June only 6·7 per cent. were males. Larval control in the cantonment, bazaars and Apozai was adequate at the time and it appeared that the majority of the catch was coming from the Zhob River 3 to 3½ miles from the nearest military lines. In the Zhob River, intense breeding of *A. stephensi* was found. In May 1945 the author revisited Fort Sandeman. He again found intense anopheline breeding in the Zhob River, *A. maculatus*, *A. stephensi*, *A. culicifacies*, *A. turkhudi* and *A. fluviatilis* being identified. Fort Sandeman continues to show a high malaria incidence, in spite of ample supplies of pyrethrum and DDT, but the autumn peak of *P. falciparum* infections has been very much reduced.

Norman White.

HARPER, P. A. ; LISANSKY, E. T. ; SASSE, B. E. ; DOWNS, W. G. ; OMAN, P. W. ; CHRISTENSON, L. D. ; LEVINE, N. D. **Malaria and other Insect-borne Diseases in the South Pacific Campaign, 1942–1945. A Series of Four Papers. I. General Aspects and Control Measures** [HARPER, LISANSKY & SASSE]. *Suppl. to Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, iii+1–67, 1 map, 3 charts & 9 figs. [22 refs.]. **II. Epidemiology of Insect-borne Diseases in Army Troops** [DOWNS, HARPER & LISANSKY]. *Ibid.* 69–89, 12 graphs. **III. Entomology** [OMAN & CHRISTENSON]. *Ibid.* 91–117, 5 figs. **IV. Parasitological Observations on Malaria in Natives** [LEVINE & HARPER]. *Ibid.* 119–28, 1 fig.

This Supplement to the *American Journal of Tropical Medicine* contains four papers by officers of the Medical Corps or Sanitary Corps of the United

States Army. Together they constitute a comprehensive survey of the incidence of malaria in the United States Forces, and of the malaria control programme in the South Pacific area during World War II. Other insect-borne diseases are more briefly discussed.

Malaria caused more than five times as many casualties as did combat, in the South Pacific. The most severe epidemics were experienced in Efate and Guadalcanal, where the maximum monthly incidence was 2,678 (April 1942) and 1,781 (November 1942), per thousand per annum, respectively. Severe but lesser outbreaks were experienced in Espiritu Santo, Tulagi-Florida, Russell Islands and Munda, New Georgia. There was no serious outbreak in either Treasury Island, Bougainville Island, Green Island or Emirau Island; these were the last four bases to be occupied. Early in the campaign the urgent military situation and shortage of supplies, coupled with a lack of appreciation of the magnitude and gravity of the malaria problem, precluded effective anti-malaria measures. The subsequent development of the South Pacific Malaria and Insect Control Organization is described: it achieved remarkable results.

In view of the extensive literature concerned with the important part played by mepacrine in the control of clinical malaria in the South Pacific, it is interesting to read "It cannot be emphasized too strongly that the control of malaria in the South Pacific resulted from the reduction of anopheline mosquito populations because of field control mesaures on all malarious bases" (p. 88). "Field control measures directed against disease bearing insects are the basis of any sound program. Suppressive drug therapy and other individual protective action are auxiliary measures of varying value" (p. 89). [This statement hardly does justice to the contribution of mepacrine to the allied victory.]

Anopheles farauti is probably the only important malaria vector in the South Pacific area. *A. punctulatus*, *A. lungae*, *A. koliensis*, *A. solomonis* and *A. nataliae* were rarely sufficiently numerous to play any important rôle; moreover, they are all zoophilic except *A. koliensis*, which is markedly anthropophilic. *A. farauti* accommodates itself to a very great variety of breeding places. It seems possible that there are two races of *A. farauti* on Guadalcanal, domestic and wild; the latter in captivity does not feed readily on man.

Aëdes aegypti was responsible for dengue outbreaks in New Caledonia, Efate, Espiritu Santo and Tulagi-Florida. *Aëdes scutellaris* may at times transmit dengue.

In the Polynesian islands filariasis is transmitted by *Aëdes pseudoscutellaris*. In the New Hebrides and Solomons the vectors are anopheline, chiefly *A. farauti* and probably *A. koliensis*. Nocturnal periodicity of microfilariae was noted on Guadalcanal, Espiritu Santo and Emirau, but not in Samoa or Fiji.

Scrub typhus was encountered in Espiritu Santo, Bougainville, and Munda (New Georgia). Only on Bougainville was there evidence of any considerable reservoir of infection.

[Many of the results of investigations recorded have been published elsewhere, but these papers do much more than record results; they present an area-wide perspective of the elaborate malaria control programme. It is a remarkable story of very great interest.] *Norman White.*

DAVEY, D. G. **Concerning Exoerythrocytic Forms and the Evidence for their Existence in Human Malaria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Oct., v. 40, No. 2, 171–82. [35 refs.]

This suggestive paper should be read in the original in order to obtain a clear idea of the problems concerning the potential existence of exo-erythrocytic forms of the human malarial parasites. The situation is reviewed chiefly from

the chemo-therapeutic angle, and only species associated with this work come under discussion.

The argument is based on the assumption that no indisputable microscopical evidence has yet been produced denoting the presence of exo-erythrocytic forms in human malaria. One explanation of this failure may be that such forms exist only during short and special periods in the infection—as is the case with some of the avian parasites.

Indirect evidence is very strong. The Cairns work of FAIRLEY *et al.* [this *Bulletin*, 1945, v. 42, 630; 1946, v. 43, 527] demonstrated a constant negative blood phase following the inoculation of very large numbers of sporozoites (except for the half-day following injection), and the author assumes from this, that wherever else the sporozoites develop, they do not develop in the red blood corpuscles. [This is perhaps not absolutely certain—it is just possible that they may be in the erythrocytes hidden in stagnant sinuses of the body. Compare, for instance, the behaviour of the ordinary schizont of *P. falciparum* and more particularly the slowly developing crescent.]

The evidence from therapeutic experiments is striking. Plasmoquine, proseptasine and paludrine all act as causal prophylactics, unlike the other anti-malarial drugs, and these three substances are known to have a special action on the exo-erythrocytic forms in avian malaria. Then there is the curious difference in the effect of quinine on blood-induced and sporozoite-induced *P. vivax* infections—effective with the former and not on the latter.

Finally, the author quoted the probable number of generations of pre-erythrocytic parasites in different species—*P. gallinaceum* 2 (or 1), *P. cathemerium* 2; not more than 3 in *P. falciparum* and not more than 4 in *P. vivax*.

P. C. C. Garnham.

DUBIN, I. N. **Bodies suggesting Exoerythrocytic Forms of *Plasmodium vivax* in Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1947, June, v. 65, No. 2, 154–6, 4 figs. [12 refs.]

Tissue cultures were made of sternal bone marrow obtained from patients who had been bitten four to six days earlier by mosquitoes infected with *P. vivax*.

In one culture, four days old, bodies resembling exo-erythrocytic forms were found in the macrophages; 50 oval and round bodies around a central nucleus were seen in one cell, and in a second, a "cluster of segmenters" with a central core.

[The paper is illustrated with four photo-micrographs, but without seeing the actual preparations, it is impossible to give an opinion about the nature of these bodies. The author himself judges them conservatively.]

P. C. C. Garnham.

MASILLAMINI, S. G. **Premature Rupture in Schizogony; an Explanation for Multiple Infection of Red Blood Corpuscles with Malaria Parasites.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 107–10.

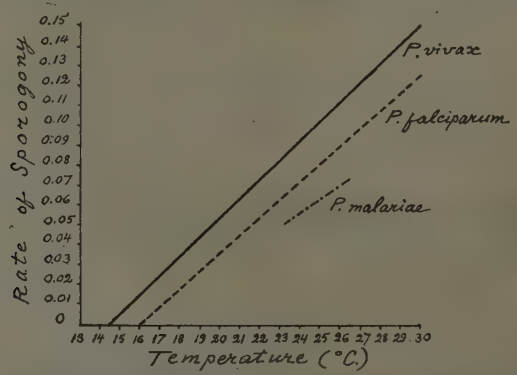
Multiple infection of red blood cells are common in malaria, particularly in *P. falciparum* infections, and are usually considered to be the result of several merozoites penetrating the erythrocyte. Binary fission is an alternative explanation and superficially appears to be likely, because strands of cytoplasm connecting the two parasites are sometimes visible. The author puts forward the theory that such appearances are due to invasion of the cell by two incompletely separated merozoites from a malformed schizont. The connecting strand may then either disappear or remain. [This is an interesting supposition and fits in well with the facts. "Ragged" schizonts are particularly common in

P. falciparum infections and what appear to be "dividing" rings are occasionally seen. It is possible, however, that the latter appearance may be a tenuiform phenomenon.] *P. C. C. Garnham.*

MOSHKOVSKI, S. D. [**On the relation between Temperature and the Rate of Development of the Malarial Plasmodia in the Mosquito. Communication I.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946 [1947], v. 15, No. 6, 19–28, 5 figs. [13 refs.] [In Russian.]

The existing data regarding the influence of temperature on the rate of the development of malaria parasites in the mosquito are based entirely on empirical observations, and no attempt has been made to correlate the rate of development with temperature. The author has made a statistical analysis of the available figures with the view to determining the laws governing this process, and has arrived at a graphical expression of the correlation between sporogony and temperature. This correlation agrees with Bodenheimer's formula, according to which the product of the duration of development and the so-called "effective" temperature is constant for each point of a curve correlating the duration of development with temperature. ["Effective" temperature denotes the difference between the observed temperature and the lowest temperature threshold for a given process.]

A calculation of the rate of sporogony based on published figures shows that the distribution of points corresponding to the rates of development at various temperatures can be described as a straight line, which can be defined by two characters—by the position of the point of its intersection with one of the axes, and by its incline. In the case of the points under discussion the point of intersection with the abscissa corresponds to the temperature threshold, representing the temperature at which there is no development of the parasite, *i.e.* the rate of the process is zero. The incline of the line denotes the steepness of changes in the rate of the process at different temperatures. This correlation can be expressed by the equation $y=b\ (t-a)$, where y=rate of the process, t=temperature, a=point of intersection of the line and the abscissa, b=tangent of acute angle formed by the straight line and the abscissa and representing the degree of the incline of the straight line. The accompanying diagram represents the



Curve illustrating the relationship between rate of sporogony and temperature for *P. vivax*, *P. falciparum* and *P. malariae*.

relationship between the rate of development (ordinate) in fractions of the duration of the process, taking 24 hours as a unit, on the one hand, and the

temperature (abscissa), on the other hand, for *P. vivax*, *P. falciparum* and *P. malariae*. From these observations it is seen that the threshold temperature for the M.T. parasite (16°C.) is higher than that for the B.T. parasite (14·5°C.), while the angle of incline is similar in both species. The above equation applied to these parasites is as follows : $y=0{\cdot}95\ (t-14{\cdot}5)$ for *P. vivax* ; $y=0{\cdot}9\ (t-16)$ for *P. falciparum*. The data for the quartan parasite are incomplete, owing to the paucity of observations.

The author has also analysed the effect of temperature on the rate of digestion of blood by mosquitoes. This relationship can also be described by a straight line, which shows that the threshold temperature is 9·9°C., while its incline is considerably steeper than that of the lines representing the effect of temperature on the development of the malaria parasites. *C. A. Hoare.*

PLETNEV, E. A. [**Bloodsucking Mosquitoes (Culicidae) of Southern Kazakhstan.**] *Izv. kazahk. Fil. Akad. Nauk.* Alma-Ata. (Ser. zool.) 1943, No. 2, 5–22. [16 refs.] [In Russian. English summary p. 126.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1947, July, v. 35, Pt. 7, 110.]

Malaria is common in Kazakstan, and mosquitoes are troublesome pests of man and domestic animals in the irrigated zone and along rivers. A survey to ascertain the species present was carried out in 1926–29 in southern Kazakstan in the area between the town of Kopal in the east and the river Suir-Dar'ya in the west and up the basin of the latter from the border of Uzbekistan to the town of Kzuil-Orda. The character of the country is described, with special reference to the various types of water in which mosquitoes bred, and notes are given on the local distribution, abundance, seasonal occurrence, breeding places and mode of hibernation of the 23 species and varieties collected. Of the Anophelines, *Anopheles hyrcanus* var. *pseudopictus*, Grassi, which was the commonest, bred in soft river water, lakes and swamps, and hibernated in the adult stage among reeds and fallen trees. Except for var. *sacharovi*, Favr, which was widely distributed, *A. maculipennis*, Mg., was not common. It bred in shallow water among pebbles, and hibernated in inhabited rooms, basements, cellars and animal quarters ; var. *sacharovi* bred in stagnant water and hibernated in animal quarters and uninhabited buildings and also among dense vegetation in gardens. *A. superpictus*, Grassi, which occurred near the mountains, bred chiefly in hard water among pebbles at the edges of springs, and hibernated in animal quarters and poultry houses and to some extent in dwellings. *A. claviger*, Mg. (*bifurcatus*, auct.) was found only in the mountains, where it bred in ponds, lakes and pits in gardens. It hibernated in the adult stage in clefts in ravines and among fallen trees, and probably also in the larval stage. *A. pulcherrimus*, Theo., was restricted to a single locality in the south-west, where it was the commonest Anopheline ; it bred in the smaller, slow-flowing irrigation ditches, and the larvae overwintered.

Comparative lists are given of the mosquitoes of southern Kazakstan and of neighbouring parts of Asiatic Russia, and the faunistic affinities of the area are briefly discussed.

VEL'TISHCHEV, P. A. [**Contribution to the Question of the Distribution of the Representatives of the Genus *Anopheles* (Diptera, Culicidae) in the Northern Part of Southern Kazakhstan.**] *Izv. kazakh. Fil. Akad. Nauk.* Alma-Ata. (Ser. zool.). 1943, No. 2, 23–9. [10 refs.] [In Russian. English summary, p. 126.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1947, July, v. 35, Pt. 7, 111.]

An account is given of investigations on the Anophelines of southern Kazakstan carried out in July–August 1937 near the town of Kazalinsk, on the

upper Suir-Dar'ya, and in the village of Dzhulek, some 60 miles south of Kzuil-Orda, further down the river. *Anopheles maculipennis*, Mg., was common in the town, where it attacked man, and var. *sacharovi*, Favr, was the most numerous Anopheline in the village. The larvae and pupae of this variety occurred in many types of water and were commonest in rice-fields, and the adults congregated in dark corners in cattle sheds and stables. The females fed almost exclusively on cattle and horses, but rarely attacked them outdoors. Very few were observed in dwellings, and they did not attack man indoors, outdoors or in the animal quarters. In experiments in which some hundreds of unfed females were released in rooms in which many people were sleeping, they were recaptured in the morning in the same unfed condition, whereas 80–100 per cent. of those taken in a cattle shed near-by contained blood. *A. hyrcanus*, Pall., which readily attacked man, was the next in abundance in the village, but did not occur in the town. Only single adults were taken in animal quarters, and the majority concentrated on the windows and walls on the sunny side of houses. *A. algeriensis*, Theo., was rare but readily attacked man after sunset in woods in water meadows ; six larvae were found in June among reeds in water with a temperature of 17·2°C. [63°F.]. Two engorged females of *A. pulcherrimus*, Theo., were taken on the railway station at Kazalinsk, and a few of *A. superpictus*, Grassi, along the railway line ; both had probably been accidentally brought by train. *A. claviger*, Mg. (*bifurcatus*, auct.) was not found, though it had been recorded from the area previously. Observation showed that the adults of *A. algeriensis*, flew little more than half a mile from their breeding places while *A. m. sacharovi* and *A. hyrcanus* covered distances of up to 5 miles. Malaria was not epidemic in the areas surveyed and was rare in some parts.

WHITE, R. Senior. **On Malaria Transmission in East Central India : Further Data.** *J. Malaria Inst. of India.* 1946, Dec., v. 6, No. 4, 469–88. [14 refs.]

Between 1937 and 1943 the author, either alone or with collaborators, published ten papers giving the results of mosquito dissections which determined the malaria vectors over an area of some 170,000 square miles served by the Bengal Nagpur Railway, between 80° and 88° East, and 18° and 24° North. This area includes the Jeypore Hills, the Singhbhum Hills, the Chikla Lake, the Orissa Coastal Plain, the Eastern Satpura Ranges, the Hazaribagh Ranges, and the Coastal Area around Vizagapatam. The success of species-control programmes has since confirmed the validity of conclusions drawn. The present paper gives the results of further extensive dissection work carried out since previous publication. A newly investigated area in the Southern Central Provinces is briefly reported on. Here *A. fluviatilis* was the only species found infected in 1945. *Norman White.*

TOFFALETI, J. P. & KING, W. V. **Some Records of Mosquito Dissections in Northern New Guinea.** *J. National Malaria Soc.* 1947, Mar., v. 6, No. 1, 32–6.

" Sporozoites of malaria parasites were found in the salivary glands of two specimens of the ' intermediate ' form of the *punctulatus* series of *Anopheles*, among 138 gland dissections of specimens of this form collected in native villages in the Hollandia area of northern New Guinea. This is the first record so far as known of infection in this form, which was the predominating one in

these villages. Gland examinations of 12 specimens of subspecies *punctulatus* and 36 *farauti* (formerly known as *moluccensis*) were negative. No infections were found in a series of 119 *A. karwari* obtained from a military camp located several miles from any native village.

" Filaria infections were found in the thoracic muscles or head of 20 of 203 specimens of the *punctulatus* series, or an infection rate of about ten per cent. Seven of the specimens (representing each of the three forms) contained matured larvae. Six individuals among 268 *Armigeres ? obturbans* and one among 13 *Aëdes* (*Aëdes*) sp. contained immature filariae in the thoracic muscles. Small numbers of nine other culicine species were negative."

VARGAS, L. El *Anopheles darlingi* Root, 1926 en Mexico. [*Anopheles darlingi* **in Mexico.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1946, Dec., v. 7, No. 4, 221–6. [10 refs.] [Summary in English by the author.]

" *Anopheles* (*Nyssorhynchus*) *darlingi* Root, 1926 is one of the most dangerous vectors of malaria in the New World ; was found in British Honduras and Guatemala by Komp (1940), in the border of Guatemala and Mexico by Kumm, Bustamante and Herrera (1943, 1943a) and now is reported from Teapa, Tabasco. As this late locality is within a zone going from Tampico, Tamaulipas to Champoton, Campeche, it is probable that the geographical distribution of the species is larger than actually reported."

ZERMATI, M. & VARGUES, R. Concentration alexique du sang au cours du paludisme aigu. [**Concentration of Complement in the Blood during Acute Malaria.**] *C. R. Soc. Biol.* 1947, Apr., v. 141, Nos. 7/8, 406–7.

A number of workers in the past have recorded a diminution, and even an actual disappearance, of complement during the course of malaria, and its more or less rapid restoration after cure of the disease.

The authors have studied the complement levels in 120 patients suffering from malaria : of these infections, 37 were *P. vivax*, 75 were *P. falciparum*, 6 were double infections of these two species and 2 were caused by *P. malariae*.

They conclude that the complement titre corresponds with the clinical state, falling during the disease and returning to normal upon recovery. In severe, and especially comatose, cases, persistent absence of complement, despite treatment, indicated a fatal termination ; conversely, a progressive rise in titre preceded cure. In benign attacks, the curve differed in primary infections and relapses : in the former case, the titre rose slightly until the 5th day and then fell ; in relapses, the curve varied inversely with the temperature.

They also observed a difference in the complement in relation to the species of parasite : the decrease in complement was slight in *vivax* infections, but very marked in the case of *falciparum*. There appeared to be some relation between the degree of parasitaemia and the complement concentration. There was also a parallelism between complement and protein levels. The authors give reason for believing that this reduction of complement in malaria is not a non-specific phenomenon, since it may not occur in other conditions involving profound protein disequilibrium. They believe the " *hypoalexie* " to be brought about by a double mechanism—disturbance of complement formation and complement fixation *in vivo* ; arguments, based on experiments, are given in support of this view. They finally conclude that among the infective diseases malaria, like other conditions due to blood parasites, belongs to a group of " *affections hypoalexiques* ", having the dual mechanism suggested above.

H. J. O'D. Burke-Gaffney.

BELTRÁN, E. & DÁVALOS, A. Posibilidades y limitaciones del examen en fresco en el diagnóstico del paludismo. [**Possibilities and Limitations of Examination of Fresh Blood for the Diagnosis of Malaria.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1946, Dec., v. 7, No. 4, 251–4. English summary (7 lines).

The authors examined 155 samples of blood for diagnosis of malaria, by the use of fresh unstained blood and compared this method with stained thick drops and thin smears. By all methods, 123 specimens were negative, 25 showed *P. vivax* and one each showed *P. malariae* and a mixed infection with *P. vivax* and *P. falciparum* respectively.

The only difference between the three methods was that while the stained smears, both thick and thin, revealed *P. falciparum* alone in 5 cases, the fresh drop only showed this species in 3.

The stained thick and thin smears thus revealed parasites in 32 cases, and the unstained fresh drop in 30.

It is suggested that fresh blood examination is efficient as an emergency measure when, for any reason, stained preparations are not available.

H. J. O'D. Burke-Gaffney.

VAN DER KUYP, E. **Pulse and Respiratory Frequency in Malaria.** *Nederl. Tijdschr. v. Geneesk.* 1947, Mar. 29, v. 91, 735. [Summary taken from *J. Amer. Med. Ass.* 1947, July 26, v. 134, No. 13, 1136.]

Van der Kuyp reviews observations on the temperature, pulse rate and respiration of 130 patients with quartan malaria and of patients with tertian or subtertian malaria observed at a hospital in Paramaribo. Pulse and respiration curves showed the quartan, tertian or subtertian type more constantly and more clearly than did the temperature curves. The three curves often supplemented one another in such a way as to make the type of fever clear. The pulse curve sometimes showed the existence of a duplex or triplex quartan infection. During treatment the temperature was the first to become normal. In patients in whom the pulse and respiration did not become normal, a relapse followed. The characteristic course suggests that schizogony on a small scale is responsible for the changes in pulse rate and respiration, because the quantity of liberated toxins is too small to influence the temperature but large enough to influence the pulse and respiratory rate, these being more sensitive to these toxins.

KIEBL, E. & SIEDEK, H. Provokatorische und therapeutische Wirkungen des Kongorots bei Malaria tertiana. [**Provocative and Therapeutic Action of Congo Red in Tertian Malaria.**] *Wien. klin. Woch.* 1947, Feb. 28, v. 59, No. 8, 123–4. [41 refs.]

On the analogy of work carried out in *P. gallinaceum* infections, it would appear that endothelial forms of *P. vivax* develop from the blood forms; that damage to the reticulo-endothelial system favours the output of endothelial forms, and that the persistence of these is responsible for subsequent relapse; hence the Ascoli method of throwing out parasites from the spleen and the reticulo-endothelial system into the blood-stream.

Injection of Congo-red, 10 cc. of 1 per cent. solution intravenously, especially if repeated, has such an action and it was thought possible that by increasing its action on the r.e.s. it might lead to complete destruction of the plasmodia and perhaps forestall and prevent the production of endothelial forms. Congo-red differs, however, from other provocatives in having no action on the circulation. The authors claim that, given with atebrin and plasmoquine, it can prevent relapse in tertian malaria. *H. Harold Scott.*

ENGSTROM, W. W., GORDON, H. H., MARBLE, A. & BRUNSTING, H. A. **Induced Malaria of Foreign Origin.** *Arch. Intern. Med.* 1947, Feb., v. 79, No. 2, 185–202, 6 figs. [Refs. in footnotes.]

This report concerns 243 patients suffering from neuro-syphilis, of whom 175 were white and 68 negroes. They were treated with malaria therapy. For this purpose 4 strains of *P. vivax* from Guadalcanal, 8 from New Guinea and 3 from the Mediterranean area were used. Mosquito transmission was attempted in 101 white patients and 23 Negroes: 99 per cent. of the white patients were successfully infected, but only 17 per cent. of the Negroes. Seventy-one patients were inoculated with blood containing trophozoites of the same strains of *P. vivax* and 48 Negro and 3 white patients were inoculated with blood containing a Trinidad strain of *P. malariae*.

The prepatent and incubation periods of *P. vivax* malaria averaged about 2 weeks when mosquitoes, and 5 days when blood inoculations, were used in the transmission of infection. Sixty-five per cent. of patients infected by mosquito-bite with Pacific strains of *P. vivax* had relapses: no relapse was observed among patients who had been inoculated intravenously with blood containing the same strains.

P. malariae infections had a tendency to cause serious renal complications.

Norman White.

BELTRÁN, E. & SANDOVAL C., A. Reducción controlada del periodo de incubación en las inoculaciones artificiales con *Plasmodium vivax*. [**Controlled Reduction of the Incubation Period in Artificially Induced Infections by** *Plasmodium vivax*.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1946, Dec., v. 7, No. 4, 255–64, 2 graphs. Summary in English by the authors.

"The relative influence of blood groups and number of parasites inoculated in artificially induced infections by *Plasmodium vivax*, were investigated in relation to the incubation period. Both factors are important, but the former has more importance than the latter. The incubation period, using incompatible bloods, even with large inocula of near 400,000,000 parasites, was never shorter than 5 days. Using compatible bloods and inocula with 100,000,000 or more parasites, the incubation period was one day only in 50 per cent. of the cases; from one to two days in 75 per cent.; and of no more than three days in all cases. From the viewpoint of economy, and in order to facilitate the hospital or nursing care of malariotherapy cases, it is advisable to use as a routine therapeutic measure, inoculation with compatible bloods, and with not less than 150,000,000 parasites."

BRAITHWAITE, P. **Some Observations on Blood Transfusion in a Highly Malarious Area.** *Med. J. Australia.* 1947, June 14, v. 1, No. 24, 725–6.

The author, who served in a military Forward Surgical Unit in the Aitape-Wewak area, discusses his considerable experience of blood-transfusion of casualties in a malarious area. A "transfusion" in this case is defined as a unit of 1 litre, when stored blood was used, and 1,400 ml. when the blood was taken from local donors, All the malaria which occurred was subtertian; the rare *P. vivax* infections were always accompanied by *P. falciparum* as well. Five methods of suppressing, minimizing or preventing malaria after blood transfusion were studied, namely (1) the use of stored blood from non-malarious areas, (2) selection of donors apparently free from malaria, (3) premedication of donors with mepacrine, (4) administration of large quantities of mepacrine to the recipients, (5) routine treatment of malaria after transfusion.

The first step was abandoned when all the 8 transfusions given in the field were followed by rigors. The blood was obtained from Sydney, and despite good air communication and packing in ice the blood was severely shaken in its transit from the hospital to the field ; it was necessary to store it for longer than a week, at temperatures well above 4°C.

Donors were selected as far as possible from those who had never suffered from overt malaria and who showed a negative thick blood-film ; but there was little doubt that most of the troops in the area had suppressed malaria. Hence, when possible, all donors were given 0·3 gm. of mepacrine four hours before their blood was taken, in addition to their routine suppressive doses. In practice, this was not always feasible in a forward area where donors and an urgent casualty often arrived together.

Experiments showed that the mean mepacrine level in the plasma of 100 men who had taken 0·1 gm. daily for 6 weeks was 21 microgrammes per litre, and this was usually sufficient to suppress malaria. In those who had taken 0·2 gm. daily, the level was 42 microgrammes per litre ; with an additional dose of 0·3 gm. the plasma level after four hours would be 47 microgrammes per litre ; but experiments suggest that no level sufficient to prevent transmission of malaria could be attained in practice if the donors' blood contained asexual parasites. The casualties themselves received 0·5 gm. of mepacrine by mouth on admission and again the next morning ; transfusion usually took place in the interval. Where necessary, the intramuscular route was employed.

These measures were fairly satisfactory when the weekly malaria rate was low : for example in March 1945, the rate was 0·4 per 1,000 and 0·2 gm. of mepacrine was being taken daily. Nine transfusions were given and one man developed overt malaria ; he had been very seriously injured.

In June and July the average weekly malaria rate was 22 per 1,000 : despite the daily suppressive mepacrine, parasites were found in the blood of 14 out of 40 apparently healthy soldiers of all ranks, sampled at random.

The second, third and fourth precautions were taken, yet 8 of the casualties transfused developed malaria ; all had been seriously wounded. It is pointed out that previous experimental work has been concerned with transfusion of non-malarious patients from malarious donors. In active service, under highly malarious conditions, the seriously wounded are themselves likely to be more potentially malarious than the donors.

Following the failure of solely suppressive measures, these were accompanied thereafter by routine malaria treatment of the patient either immediately before or after the transfusion. When this was done, none of the further 27 patients transfused developed overt malaria. It is stated that, despite the disadvantages of indiscriminate treatment in these cases, it not only prevents malaria, but also acts as a tonic for those casualties on the brink of a malarial attack.

The routine course consisted of 40 grains of quinine daily for the first 3 days ; 0·6 gm. of mepacrine on the 4th and 5th days ; 0·4 gm. on the 6th to 9th days, and on the 10th to the 12th days the patients were given daily 0·2 gm. of mepacrine, and 0·02 gm. of plasmoquine. *H. J. O'D. Burke-Gaffney.*

RAYMOND, W. D. **Totaquina and its Rivals.** *East African Med. J.* 1946, Oct., v. 23, No. 10, 301–10, 12 figs.

In this paper read before a Branch of the B.M.A. at Dar es Salaam the lecturer describes the preparation of totaquina carried out there during the war from indigenous supplies of cinchona bark. Brief mention is made of the introduction of this bark to Europe and to its use in the treatment of malaria. Quinine accounts for 40 per cent. of total alkaloidal content in the commoner species

of cinchona and came to be regarded as the most suitable of these alkaloids in the treatment of malaria before the advent of synthetic drugs. Subsequent work has shown that the dominant position of quinine arose by chance rather than on account of intrinsic merit. In order to make available a cheap preparation in which the other alkaloidal constituents of cinchona bark could be employed, the Malaria Commission of the League of Nations recommended the preparation of totaquina. It was included in the B.P. of 1932, where it was defined as a mixture of cinchona alkaloids containing at least 70 per cent. which were crystallizable, not less than 20 per cent. of these being quinine. Two preparations of totaquina came into use, Type I being prepared from the total alkaloids of a suitable bark, and Type II from residues to which the requisite amount of quinine was added. Totaquina contains not salts but the alkaloidal free bases. The product prepared in Dar es Salaam had the following composition: quinine 40 per cent.; cinchonidine, 20; cinchonine, 10; quinidine, 1; amorphous alkaloids, 20; moisture and ash, 9 per cent. The difficulties met with in the erection of a plant for commercial preparation with the aid of local resources are outlined. By the end of 1942, about 640 lb. of totaquina had been produced and in 1945 the annual output was 8,500 lb., which was used to supply neighbouring territories in East Africa. Steps are still being taken to improve the quality of the product. Whether it will be able to compete successfully with the newer synthetic products which are dealt with in the lecture will probably depend largely on local conditions.

J. D. Fulton.

Gordon, H. H., Dieuaide, F. R., Marble, A., Christianson, H. B. & Dahl, L. K. **Treatment of *Plasmodium vivax* Malaria of Foreign Origin. A Comparison of various Drugs.** *Arch. Intern. Med.* 1947, Apr., v. 79, No. 4, 365–80, 2 charts. [Refs. in footnotes.]

The drugs used in this series of observations were: quinine sulphate, 16 or 30 gm. over a period of 7 or 14 days; quinacrine hydrochloride (mepacrine), 3·2, 2·6 or 1·2 gm. over a period of 7, 6 or 1 days; SN 6911 (3-methyl-4-[4-diethylamino-1-methylbutylamino]-7-chloroquinoline)—both the bisulphate and dinaphthoate salts of SN 6911 were used, 3·2 gm. over a period of 7 days; chloroquine, 2·0, 0·8, 1·0 or 1·2 gm. over a period of 6, 6, 1 or 3 days; and SN 8137 (4-[3-diethyl-amino-2-hydroxypropylamino]-7-chloroquinoline), 2·0 gm. in 3 days. In all cases relatively large doses were given on the first day of treatment.

All the patients were white soldiers who had contracted *P. vivax* malaria in either the Pacific or the Mediterranean area and who suffered from relapse (or delayed primary attack) while under observation in the Harmon General Hospital.

All the synthetic drugs were effective in controlling fever and parasitaemia, in which respect they are superior to quinine sulphate. Minor toxic symptoms were few. Neither SN 6911 nor chloroquine showed any superiority over quinacrine in preventing relapse, and there are indications that SN 8137 will prove to be equally ineffective in this respect. None of the three newer drugs causes the skin discoloration that quinacrine does. They may, therefore, be valuable substitutes for quinacrine in treatment of the acute attack, especially in the few patients who have a sensitivity to the latter drug.

Norman White.

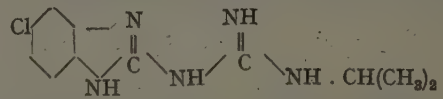
Russell, B. **Mepacrine Eruptions. A Case in the British Isles.** *Lancet.* 1947, Aug. 9, 205–6.

DAME, L. R. **The Effects of Atabrine on the Human Visual System.** *Amer. J. Ophthalm.* 1946, Nov., v. 29, No. 11, 1432–4.

Apart from minor and temporary scotomas and blind-spot-enlargement which occurred when high blood-mepacrine levels were suddenly attained, no visual changes were found during brief or prolonged administration of the drug to volunteers. *H. J. O'D. Burke-Gaffney.*

ACHESON, R. M., KING, F. E. & SPENSLEY, P. C. **Benziminazoles related to Paludrine.** [Correspondence.] *Nature.* 1947, July 12, 53.

The differences in activity of paludrine recently noted by HAWKING [this *Bulletin*, 1947, v. 44, 648] when it is added directly in solution to tissue cultures of *P. gallinaceum* and *P. cynomolgi*, and in the sera of animals treated with the drug, led him to suggest that the substance had been activated *in vivo*. The present authors have prepared a guanidinobenziminazole, of the formula :—



which, from considerations of spatial relationships, might have been formed from paludrine in the body by the loss of two hydrogen atoms. Benziminazole derivatives are, moreover, known to inhibit the growth of certain micro-organisms. The new substance resembled paludrine in chemical properties, including the formation of a copper complex [see this *Bulletin*, 1947, v. 44, 283]. However, it and related compounds proved inactive against *P. gallinaceum* infections in chickens, and the conversion of paludrine in the body to either of the synthetic substances prepared can therefore be excluded. *J. D. Fulton.*

KOEPFLI, J. B., MEAD, J. F. & BROCKMAN, J. A., Jr. **An Alkaloid with High Antimalarial Activity from** *Dichroa febrifuga.* [Correspondence.] *J. Amer. Chem. Soc.* 1947, July, v. 69, No. 7, 1837.

[See this *Bulletin*, 1947, v. 44, 699.]

BERNSTEIN, J., STEARNS, Barbara, DEXTER, M. & LOTT, W. A. **I. Derivatives of Aminopyridines.** *J. Amer. Chem. Soc.* 1947, May, v. 69, No. 5, 1147–50. [Refs. in footnotes.]

BERNSTEIN, J., STEARNS, Barbara, SHAW, E. & LOTT, W. A. **II. Derivatives of 2,6-Diaminopyridine.** *J. Amer. Chem. Soc.* 1947, May, v. 69, No. 5, 1151–8. [Refs. in footnotes.]

BERNSTEIN, J., PRIBYL, E. J., LOSEE, Kathryn & LOTT, W. A. **III. Some Substituted Sulfanilamidopyridines.** *J. Amer. Chem. Soc.* 1947, May, v. 69, No. 5, 1158–60.

CURD, F. H. S., DAVIS, M. I., HOGGARTH, E. & ROSE, F. L. **Synthetic Antimalarials. Part XV. Some Aryloxy- and Arylthio-dialkylaminoalkylaminopyrimidines.** *J. Chem. Soc.* 1947, June, 783–90.

CURD, F. H. S., LANDQUIST, J. K. & ROSE, F. L. **Synthetic Antimalarials. Part XIV. Some 2-Arylamino-4-aminoalkylaminoquinazolines.** *J. Chem. Soc.* 1947, June, 775–83.

ELDERFIELD, R. C., KREMER, C. B., KUPCHAN, S. M., BIRSTEIN, O. & CORTES, Gloria. **Synthesis of certain 8-(5-Alkylamino-1-methylpentylamino)-Derivatives of Quinoline.** *J. Amer. Chem. Soc.* 1947, June, v. 69, No. 6, 1258–60. [Refs. in footnotes.]

DE MENDONÇA, F. C. & CERQUEIRA, N. L. **Insects and other Arthropods captured by the Brazilian Sanitary Service on Landplanes or Seaplanes arriving in Brazil between January 1942 and December 1945.** *Bol. Oficina Sanitaria Panamericana.* 1947, Jan., v. 26, No. 1, 22–30.

The first phase of the campaign for the eradication of *Anopheles gambiae* from Brazil extended from 1939 to 1941, and complete success was achieved. This report concerns the second phase of the campaign, which commenced in 1942 and is still continuing. The inspection and fumigation of all aeroplanes arriving in Brazil from Africa is compulsory, not only because of the possible reintroduction of *A. gambiae* and other disease vectors, but also because of the numerous agricultural pests of Africa which might become established.

The authors give a brief account of the transfer of the organization from the Malaria Service to the Brazilian Quarantine Service, the methods of inspection and spraying, and then summarize, in three tables, the results of four years' work.

In the first table, the figures are given for the total number of arthropods encountered in flying-boats and land-planes, classified by families or orders (the mosquitoes being classified by genera and species). The figures add up to many thousands, including 352 *A. gambiae* and 4 *Glossina palpalis*.

The second table gives the numbers of machines which arrived each month, and indicates the numbers of those with *A. gambiae* on board. The greatest numbers of *A. gambiae* were found in August (21), September (75) and October (163) in 1943.

The number of aeroplanes from which arthropods, either dead or alive, were recovered between 1942 and 1945, is analysed month by month in the third table. This number (8,287), emphasizes the importance of this campaign for the prevention of the introduction of harmful insects into the country from Africa. *H. S. Leeson.*

TALIAFERRO, W. H. & TALIAFERRO, Lucy G. **Asexual Reproduction of *Plasmodium cynomolgi* in Rhesus Monkeys.** *J. Infect. Dis.* 1947, Jan.–Feb., v. 80, No. 1, 78–104, 7 figs. [24 refs.]

P. cynomolgi usually produces a non-lethal infection in rhesus monkeys which is characterized by a tertian periodicity. Both in blood- and sporozoite-induced infections, two broods of parasites often co-exist and these may be recognized by the numerical preponderance of the various stages. Unfortunately, the multinucleate forms and mature schizonts are usually rare in the peripheral blood. Segmentation under American conditions occurs between 7 and 9 a.m. on alternate days.

The normal picture is usually as follows :—

Acute rise : 5th to 7th day.
Peak and slow decline : 8th to 12th day.
Developed infection : for a further week or longer.
Latency : several months.
Relapses.

These periods are accompanied by changes in the rate of asexual reproduction, thus : *Acute rise*—Maximum number of merozoites, low death rate of parasite, normal length of asexual cycle, *i.e.* 48 hours. *Peak*—lowest number of merozoites, high death rate of parasite, extended cycle of more than 48 hours. *Developed infection*—Merozoite numbers returning to normal, high death rate of parasite, cycle again 48 hours.

The survival rate may be as high as 100 per cent. during the acute rise and it may sink to 1 per cent. in the developed infection. The picture differs from

animal to animal and according to the amount of inoculum, but, in general, resembles the above description.

The chief difference between blood and sporozoite infections was in the length of the pre-patent period—3–7 days in the former and 9–11 days in the latter.

The authors compare these phenomena with *P. brasilianum*, *P. cathemerium* and *P. floridense* infections and note the greater resemblance to the last two. They suggest that the cause of the changes in the asexual cycle at the crisis is probably the presence of some parasiticidal substance in the serum.

P. C. C. Garnham.

Indian Research Fund Association. Rep. Scient. Advisory Board for Year 1st Jan. to 31st Dec., 1946, 9–14. **Mammalian Malaria Enquiry under the Director, Central Research Institute, Kasauli.**

The malaria enquiry was undertaken in India with the object of discovering in *Plasmodium cynomolgi* of rhesus monkeys an exoerythrocytic cycle of development comparable with that occurring in avian and saurian malaria. The enquiry at the end of December 1946 had been in progress 18 months but no evidence had been obtained that an exoerythrocytic cycle occurred.

Transmission of *P. cynomolgi* was successfully carried out by a number of anophelines, the complete development having been demonstrated in *A. subpictus*, *A. annularis*, *A. culicifacies*, *A. barbirostris* and *A. hyrcanus*. *A. annularis* was chiefly used owing to its prevalence. Experience showed that sporozoites were most infective when development in the mosquito had occurred at 72°–82°F. In monkeys, the incubation period after sporozoite infection averages 15 days. In two cases, after 5 and 7 weeks, infection had apparently failed. Accordingly splenectomy was carried out and in both cases, 12 and 52 days later, attacks occurred. Observations on 90 monkeys recovered from the primary infection showed that in 15 months only two experienced true relapses.

In transmission experiments 15 cc. blood were taken from the heart 5, 10, 25, 37 and 72 minutes after sporozoite inoculation and injected intraperitoneally to other monkeys. Blood taken daily was similarly inoculated. In no case did infection occur earlier than 2 or 3 days before parasites could be detected in thick films of the blood of the sporozoite-injected monkeys. During the incubation period after sporozoite inoculation, splenectomy was performed and the entire organ or a part of it was transplanted into test monkeys or an emulsion of the spleen was inoculated intraperitoneally. In no case did the test monkeys become infected. Similar experiments with like results were carried out with liver, bone-marrow, brain, lung, kidney, suprarenal and muscle. It was thus shown that the blood is not infective at any time within the nine days following sporozoite inoculation and that tissues are similarly not infective till the blood becomes infective.

Observations were also carried out on the skin of monkeys, into which ground-up thoraces of infected mosquitoes had been injected. The skin was removed after the expiry of varying intervals—a quarter of an hour up to four days. In only one or two sections of skin, removed after an hour, were a few sporozoites seen, though calculation showed that at least 1,000 sporozoites might be expected in one high power field. It is noted that only 39 per cent. of the inoculated animals developed infection. Similar observations were made on spleens which had been implanted on the abdominal wall and into which sporozoites had been injected. Tissue removed at intervals failed to show developmental forms of the inoculated sporozoites. In this case only 50 per cent. of animals injected with sporozoites became infected. It is stated

that tissues from 136 monkeys in various stages of infection have been preserved for later examination. It is noted that formol and malarial pigments can be removed from tissues by a saturated solution of picric acid in alcohol. In one monkey, in which arterial, venous and capillary blood showed only 13 per cent. of the red cells infected, the blood in the Billroth cords in the spleen had virtually 100 per cent. of the red cells infected. A similar phenomenon was recorded by TALIAFERRO and CANNON in 1936 in a monkey infected with *P. brasilianum* [this *Bulletin*, 1937, v. 34, 622].

Attention is drawn to various structures which might lead to fallacious conclusions. Such are adventitial histiocytes which lie in the smallest vacuoles of the brain ; these are elongate cells which lie in rows or singly along the vessels of the brain and contain coarse granules which give them some resemblance to exoerythrocytic schizonts of avian malaria. There were also bodies within macrophages resulting from the phagocytosis of various objects. Cyst-like bodies 40μ in diameter and containing a large number of small structures were found in sections of the psoas muscle of one monkey with a heavy malarial infection. Their nature is unknown. Tissue cultures made from monkeys after sporozoite inoculations failed to reveal any developmental forms.

Tissues of Malabar squirrels infected with *P. ratufae* failed to show any exoerythrocytic stages. *C. M. Wenyon.*

PEEL, E. & RODHAIN, J. Contribution à l'étude des Plasmodiums des anthropoides africains. La schizogonie du *Plasmodium reichenowi* dans le sang périphérique. [**Study of *Plasmodium* in African Anthropoids. Schizogony of *Plasmodium reichenowi* in the Peripheral Blood.**] *Ann. Soc. Belge de Méd. Trop.* 1945, Dec. 31, v. 26, No. 4, 341–7, 1 pl. [10 refs.]

A chimpanzee at Léopoldville was discovered to be suffering from an intense infection of *Plasmodium reichenowi* (a parasite closely resembling *P. falciparum* of man). The blood was examined daily for a week, when the animal died of the disease. In addition to the ordinary rings and "tenue" forms, mature schizonts were found in the blood every day, though in small numbers. The merozoites numbered 12–14. Schizonts were numerous in the spleen, rare in the liver, and absent from all other organs. No gametocytes were found either before or after death.

The authors suggest that the abnormal prevalence of schizonts in the peripheral blood, and the fatal nature of the infection, were due to a loss of premunition. *P. C. C. Garnham.*

STAUBER, L. A. & WALKER, H. A. **Preparation and Properties of Erythrocyte-free Avian Plasmodia.** *Proc. Soc. Exper. Biol. & Med.* 1946, Nov., v. 63, No. 2, 223–7, 4 figs. on 1 pl. [11 refs.]

The authors have found, as others have done, that immune sera prepared in rabbits by the injection of haemolysed erythrocytes infected with avian plasmodia lose the agglutinative and precipitative antibodies when absorbed with normal uninfected erythrocytes. This has been explained by supposing that the avian plasmodia contain substances which are antigenically similar to normal erythrocytes or that haemolysis of the infected cells does not remove the erythrocytes sufficiently to eliminate their share in the production of the immune bodies. It seemed advisable, therefore, to investigate the possibility of producing suspensions of plasmodia freed entirely of the erythrocytes. After some experimentation it was found that if the suspension of infected erythrocytes, after saponin haemolysis, was subjected to enzymatic digestion at low *p*H (5–5·5) practically all trace of the erythrocytes, including their nuclei, was

dissolved, so that the washed product consisted almost entirely of spherical parasites 1μ to 7μ in diameter, together with leucocytes which appeared to be untouched by the procedures. The parasites are so unaltered morphologically that in dry films stained by Giemsa it is possible to distinguish *P. lophurae* from *P. cathemerium*. Inoculation to young ducks shows, however, that the parasites, though retaining their morphological character, are killed. For preserving the parasites as antigen they are suspended in buffered saline containing 0·2 per cent. formalin and stored in the refrigerator.

C. M. Wenyon.

Beltrán, E., Dávalos, A. & Sandoval C., A. Estudio de infecciones artificiales con *Plasmodium vivax*, en el hombre, y con *P. gallinaceum* en el pollo, en sus relaciones don los factores climáticos. [**Study of Artificial Infections with *Plasmodium vivax* in Man and *P. gallinaceum* in Chicks in relation to Climatic Factors.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1946, Dec., v. 7, No. 4, 227–36, 2 graphs. Summary in English by the author.

" Data are presented in regard to the observation over six consecutive years of 155 artificially induced human infections with *P. vivax*, and 152 artificially induced avian infections with *P. gallinaceum*.

" In the case of human vivax malaria, the results obtained although not conclusive, seem to indicate a greater severity on the infections produced in the cold and dry months (October to March) than in the warm and rainy months (April to September).

" In the case of avian malaria the results are of more difficult interpretation ; they seem to indicate that the principal factor involved in the type or character of the infection, under the particular circumstances of our experiments, was the age of the experimental animals.

" To appreciate fully the results of our observations, it is important to keep in mind that the seasons at Mexico City are not as clearly separated by sudden variations as is the case in other places of extreme climates. Therefore, it seems desirable to repeat in other localities these observations."

Meyer, Herta. **Cultivation of the Erythrocytic Form of *Plasmodium gallinaceum* in Tissue Cultures of Embryonic Chicken Brain.** [Correspondence.] *Nature.* 1947, Aug. 2, 155–6.

The author, in cultivating the exoerythrocytic form of *P. gallinaceum* in tissue cultures of embryonic chicken brain, found that proliferation of the parasites was very slow and the initial stages difficult to observe.

Embryonic chicken brain was therefore cultivated with a drop of highly infected chicken blood, first in Carrel flasks, passing later to the hanging drop method. In this way, it was possible to note parasitized cells after 3 or 4 weeks of cultivation : the parasites seen had the same form as those in cultures of the exoerythrocytic form.

Details and illustrations of these findings are to be published fully.

H. J. O'D. Burke-Gaffney.

Tullis, J. L. **The Distribution of Exoerythrocytic Parasites and the Tissue Reaction caused by Blood-Induced *Plasmodium gallinaceum* Infection in Chicks.** *Amer. J. Trop. Med.* 1947, Jan., v. 27, No. 1, 21–9, 9 figs. on 2 pls.

The intravenous inoculation of blood containing *P. gallinaceum*, into 5-day-old chicks, caused the appearance on the fourth day of small numbers of exo-erythrocytic parasites in reticulo-endothelial cells of the blood and of the white

pulp of the spleen. On the sixth day, such forms were found also in the liver, heart, lungs and intestine.

Suppressive quinine delays the appearance of exo-erythrocytic forms until the twelfth day; then for a fortnight they are plentiful in the above organs and are occasionally seen in the pancreas, fat, kidneys, bone marrow and striated muscle. Under suppressive therapy, the cytoplasm of the liver cells is solid and granular, whereas in (*a*) untreated cases, (*b*) uninfected birds, and (*c*) quinine-treated chicks in the pre-patent phase, it is clear and contains glycogen.

The histological methods include Maximow staining of sections preceded by intra-vital India ink. *P. C. C. Garnham.*

TERZIAN, L. A. **The Effect of Splenectomy on Avian Malarial Infections.** *J. Infect. Dis.* 1946, Nov.–Dec., v. 79, No. 3, 215–20.

The lymphoid-macrophage system is known to be extremely active during the course of acute malaria in warm-blooded animals, but the exact relationship between the degree of splenomegaly and parasite density is unknown. The effect of splenectomy in two series of chicks infected with (1) *P. gallinaceum* and (2) *P. lophurae* was therefore determined. Very careful controls of several kinds (including the performance of laparotomy without removing the spleen) were maintained, and it was proved conclusively that splenectomy had no effect on the course of *P. lophurae* infections. With the more virulent *P. gallinaceum*, however, splenectomy during the latent period resulted in increased parasitaemia, indicating that the remaining lymphoid-macrophage cells in the body were not quite sufficient to deal immediately with this species of parasite. *P. C. C. Garnham.*

BISHOP, Ann & BIRKETT, Betty. **Acquired Resistance to Paludrine in *Plasmodium gallinaceum*.** *Nature.* 1947, June 28, 884–5. [10 refs.]

The phenomenon of acquired drug resistance in plasmodia has previously been reported in a few instances [this *Bulletin*, 1921, v. 18, 96; 1933, v. 30, 860; 1935, v. 32, 116; 1942, v. 39, 438]. By treating chickens infected with a normal strain of *P. gallinaceum*, passaged intravenously every few days, with 0·025 mgm. paludrine per 20 gm. body weight, the present authors found that after one month of treatment double the dose of drug could be tolerated without affecting the parasites. By giving larger doses, a forty-fold increase of resistance to the drug was developed by the parasites, which were normal in appearance and produced a heavy infection in chickens receiving the maximum tolerated dose of paludrine (2 mgm. per 20 gm. daily). The development of a normal strain of parasites was completely inhibited by such dosage. The new strain was also resistant to the methyl derivative of paludrine (M 4430) but not to mepacrine. Similar treatment to the above failed to produce resistance to the latter drug, but a minimal degree of resistance was obtained with plasmoquine (pamaquin) after 8 months' treatment. Exoerythrocytic forms appeared normally in infections with the resistant strain. In contrast to the result obtained by FAIRLEY [this *Bulletin*, 1946, v. 43, 527] in the case of human malaria parasites, development of the resistant strain occurred normally in mosquitoes (*Aëdes aegypti*) which were fed on chicks receiving treatment with paludrine, and the sporozoites were infective. The stability of the resistance was unimpaired after 5 passages in mosquitoes over a period of 3 months. The mechanism of production of resistance is still a matter for speculation.

J. D. Fulton.

WILLIAMSON, J., BERTRAM, D. S. & LOURIE, E. M. **Effects of Paludrine and other Antimalarials.** *Nature.* 1947, June 28, 885–6.

Acquired resistance has been produced to paludrine in *P. gallinaceum* passaged in chickens in two series of experiments in which the host was treated with the minimum effective dose for normal parasites and with the maximum tolerated dose for chickens respectively. Resistance to the drug was first noted after 2 to 3 months in both series, and, when fully developed, the resistant strain withstood 20 to 40 times the amount tolerated by the normal strain. The new strain maintained its characters after passage through the mosquito (*Aëdes aegypti*). It was resistant to M 4430 (the methyl derivative of paludrine) but not to M 3349 or M 3502, both of which are chemically related to paludrine but, unlike the latter, contain a pyrimidine ring. The new strain was also sensitive to quinine, mepacrine and sulphadiazine and strains resistant to these substances could not be prepared. *J. D. Fulton.*

COULSTON, F. & HUFF, C. G. **The Morphology of Cryptozoites and Metacryptozoites of *Plasmodium relictum* and the relationship of these Stages to Parasitemia in Canaries and Pigeons.** *J. Infect. Dis.* 1947, Mar.–Apr., v. 80, No. 2, 209–17, 13 coloured figs. on 1 pl.

The morphology of the pre-erythrocytic stages of *P. relictum* was studied in the wing skin of canaries and pigeons, and was compared with similar stages of *P. gallinaceum*. The youngest parasites seen were 17¾ hours old and at this stage were just over 2μ in diameter. Segmenters appeared from 36 to 50 hours after inoculation of sporozoites. The parasites differed from those of *P. gallinaceum* in being smaller, having ovoid instead of crescent-shaped cryptozoic merozoites and in that the merozoites were fewer in number. Differentiation into macro- and micro-schizonts in the metacryptozoic generations was noted.

The infection in canaries and pigeons behaved quite differently. In the former there was a patent parasitaemia, in the latter the blood infection was occult or absent. Visible parasitaemia, however, occurred in pigeons following blood inoculation. *P. C. C. Garnham.*

HAWKING, F. **Growth of Protozoa in Tissue Culture. II.** *Plasmodium relictum*, **Exoerythrocytic Forms.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Oct., v. 40, No. 2, 183–8, 17 figs. (6 (4 coloured) on 2 pls.) [11 refs.]

Exoerythrocytic forms of *P. relictum* were grown in tissue culture, by means of the author's *P. gallinaceum* technique. Growth of the spleen cells of the infected canaries was not quite as satisfactory as that of ordinary chicken tissue, but the different stages could be followed. The parasites were unevenly distributed in the culture. Two types of schizonts may be distinguished, one with a fair amount of cytoplasm distributed evenly throughout the parasite, and the other with scanty cytoplasm concentrated around the chromatin. The free merozoites are elongate with one end pointed and the other blunt, and with a central sphere of chromatin. No differentiation into macro- and micro-merozoites was noticed. *P. C. C. Garnham.*

GINGRICH, W. D. & SCHOCH, Eugenia W. **Standardization of a Test for Antimalarial Effect with *Plasmodium cathemerium* in the Canary.** *J. National Malaria Soc.* 1947, Mar., v. 6, No. 1, 68–73, 3 figs.

The authors describe the standardization of an antimalarial test in canaries infected with *P. cathemerium*, one advantage of these birds being that only small amounts of drug are required for this purpose. The strain of plasmodium

used produced only mild infections and exoerythrocytic forms of the parasite were not observed. The results therefore apply only to blood forms. In one experiment, the course of blood infection was followed in stained smears after intravenous inoculation of the host with from 5 to $0{\cdot}1 \times 10^6$ parasites in 5 per cent. normal canary serum in saline. In addition, 5 birds were inoculated with $0{\cdot}5 \times 10^6$ parasites and received oral treatment with quinine dihydrochloride in doses of 0·147 mgm. twice daily for 4½ days, starting on the day of inoculation. Untreated birds which received the inoculum of ½ million parasites had a peak of parasitaemia on the fifth day, and it proved the most suitable for the test. From the data obtained the "quinine equivalent" was calculated. It is the ratio of the amount of drug to that of the minimum effective dose of quinine, namely that which will produce a reduction in the number of parasites equal to that of the latter, over the period of test. Details of calculation of the quinine equivalent based on experimental data are given for two salts of pamaquin (plasmoquine). *J. D. Fulton.*

TRYPANOSOMIASIS.

i. NIGERIA. **Annual Report Sleeping Sickness Service 1944** [McLETCHIE, J. L.]. 3 mimeographed pp.

ii. ——. **Annual Report Sleeping Sickness Service 1945** [McLETCHIE, J. L.]. 12 mimeographed pp.

iii. ——. **Annual Report Sleeping Sickness Service 1946** [McLETCHIE, J. L.]. 12 mimeographed pp.

i. Towards the end of 1944 Dr. H. M. O. LESTER ceased to be in charge of the Sleeping Sickness Service, having held this post since 1929.

During the year, staff remained on a maintenance basis, the usual distribution being 2 medical officers on sleeping sickness surveys, 2 controlling the infection among mine workers, 4 on the settlement scheme, well sinking, and tsetse control, 1 or 2 on leave, and 1 entomologist reopening his research programme. In addition there was a further assistant M.O. stationed at the Anchau Settlement.

No new areas were surveyed, but arrangements were made for mass treatment of sleeping sickness, yaws, ulcers and scabies in Ogoja Province. In re-surveys, a measure of the improved position is provided, for example, by figures for southern Zaria, where 88,000 people showed an infection rate of 2·2 per cent., as against 19 per cent. in 1936.

Six new dispensaries were built in Benue Province, and 1 in Zaria. The Service now controls 60 dispensaries, dressing stations and temporary field posts. The proportion of primary cases attending for full courses of 14 injections in dispensaries of the Benue Province is only 55 per cent., and in this province about 12 per cent. of dispensary cases relapse. The relapse rate among survey cases is much less, despite shorter treatment, because such cases are found at an earlier stage. In general, 20 per cent. of dispensary cases are relapses after previous, often inadequate, treatment.

The sleeping sickness dispensaries undertake a good deal of general work. Thus, in the 1944 epidemic of meningitis, 2,500 cases of this infection were treated by the Benue, and 1,850 by the Zaria, units. A considerable feature of the activities of sleeping sickness units is the treatment of yaws.

The protective clearance campaign affects 5 provinces. It is estimated that 49,000 people benefited by new clearings, totalling 180 miles in length, in districts of Zaria, Kano and Bauchi. In the old clearings annual growth is

light, and re-slashing is easily and efficiently done. About 400,000 people have now been protected by communal effort.

Education and propaganda are notable features, particularly in the Anchau tsetse-free corridor, and the care of new and improved villages is largely entrusted, with gratifying results, to district, village and hamlet heads. There is also an active programme for livestock improvement, including the encouragement of pig-breeding by villagers for profit. In conjunction with the Geological Survey, 31 wells were sunk in the 1943–4 season.

Research was necessarily very limited. The entomologist built a field laboratory at Rigachikun, in Zaria Province, for research mainly on *G. palpalis*. Observations have been made, but have not yet reached a stage where results may be presented, on insect repellents, on changes in the blood sedimentation rate in sleeping sickness, on pentamidine as a prophylactic among mine labourers, and on treatment with *p*-arsenosophenylbutyric acid.

ii. The staff position was similar to that of 1944, except that more officers were away on leave.

The Obudu division of Ogoja was surveyed for the first time, revealing a lower sleeping sickness rate than had been expected—1·2 per cent. among 49,610 people. Lumbar puncture was performed in all the cases diagnosed, and of the first 100 of these, 56 showed some c.s.f. abnormality; in 24 of the 56 with abnormal spinal fluids the change was slight (5–40 cells per cmm., 15–30 mgm. protein per cent.); in 32 the abnormality was greater. This differs from previous experience at initial surveys, mostly in the Northern Provinces, where it was rare to find areas in which more than a very small percentage of patients had the nervous system affected.

Calabar was surveyed, in connexion with the new Calabar-Mamfe road. Tsetse flies are present in this area, but no sleeping sickness was found among 1,832 persons examined. The infection rate at the proposed new site for the Igala division headquarters in Kabba Province was 0·35 per cent., in 1,710 people examined.

As for re-surveys, in parts of the 5 Northern Provinces, Bornu, Benue, Bauchi, Zaria and Kano, 85,000 persons were examined, revealing infection-rates of 0·3 to 1·3 per cent., as compared with 7 to 35 per cent. at the original surveys (1933–43). In one particular district in the Katsina area, in which district the original survey was followed by neither dispensary facilities nor communal clearance, an incidence of over 4 per cent. was found, and this is regarded as a potentially dangerous focus. Figures for individual Katsina hamlets ranged from 2 to 20 per cent.

Regular 6-weekly examinations are a feature of the control measures in connexion with a mines labour force of over 5,000, in the " restricted " areas of Kabba-Ilorin, Niger, and south-western Plateau Provinces. Every six weeks an average incidence of 0·67 per cent. new cases is detected. The rate among these workers in 1940 was 6 per cent.

The standard treatments now used are :—

(1) Trial dose of 0·2 gm. followed by three 1·0 gm. doses of antrypol; then five to ten 2·0 gm. doses of tryparsamide, all injections at 5-day intervals.

(2) Antrypol-tryparsamide mixture (antrypol 0·5 gm. plus tryparsamide 1·5 gm.); 6 to 15 injections at 5- or 7-day intervals, following on an initial trial dose of 0·2 gm. antrypol. This " synergic " mixture is valued in advanced or relapsed cases.

Entomological activities have included tsetse surveys in both Northern and Southern Provinces, the training of new fly boys against future needs, and preliminary tests with DDT and Gammexane.

Progress in protective clearance, by communal labour, is briefly described, for each of 5 provinces. There is no doubt as to the value of these short

(800–1,000 yards) ruthless clearings, made at points of possible high man-fly contact, along streams in the relatively arid Northern Provinces which have only a narrow fringe of thicket, Annual clearing of the regrowth represents only from a few hours' to 1 or 2 days' work per adult male. In the account of measures taken in Kano Province there is the interesting observation that groves of mangoes had been planted along relatively tsetse-free stretches of large rivers at Kauran Mata, near Kano. Fast [!] donkeys carried the fruit to Kano City. In due course epidemic trypanosomiasis decimated the donkey herds, and the groves were found to be "alive with *G. tachinoides*". Fortunately, no human epidemic arose, and the groves have now been cleared, with the exception of a stretch of 1,000 yards left for experimental purposes. Legislation is to be enacted to control the planting of low-branching shady trees along the banks of streams.

Progress in the Anchau tsetse-free corridor is described. Further long stretches of stream were cleared. Only one barrier clearance was found neglected. In all barriers there was heavy grass growth and no evidence of unusual erosion due to loss of riverine thicket. Schooling, propaganda, improvements in stock farming, encouragement of fruit and other useful tree planting, and well-sinking continue as prominent features of the settlement scheme. [This Anchau project is a striking example of bold, imaginative, and efficient planning and execution; it has not yet received the publicity and acclaim which it deserves. See this *Bulletin*, 1946, v. 43, 1022.]

Trials of *p*-arsenosophenylbutyric acid and pentamidine have continued. "They are valuable when a group of mild cases must be treated quickly and have the advantage over antrypol in that the initial injection, even of a full dose, has no serious toxic effect, and that optimal dosage can be given within a few days." For mass treatments of large numbers of cases in various, usually not precisely determined, stages of the disease, combinations of antrypol and tryparsamide are still advised.

Observations by one officer on the erythrocyte sedimentation rate have shown a characteristic and very rapid increase in sedimentation, apparently related to the well-known occurrence in sleeping sickness of auto-agglutination. A low rate probably indicates a recent infection of low virulence, and a pronounced fall in the rate after the administration of antrypol appears to be diagnostic.

iii. The staff position was even worse than in the two preceding years. Nevertheless, more than half-a-million people were examined, which is more than in any previous year of mass examination, but the number who needed treatment was much smaller in 1946 than in the previous peak year. The actual figures for the numbers of persons examined in 1943, 1944, 1945 and 1946 are 197,307; 182,914; 281,493 and 508,745 respectively. In the table below the numbers of cases treated, in each of these four years, are grouped according to the organizational circumstances under which they received treatment:—

	1943	1944	1945	1946
New surveys	5,321	Nil	624	Nil
Re-surveys		2,342	1,174	3,503
Dispensaries	13,100	10,432	10,126	9,707
Mines labour	540	475	293	277
Hospitals, etc.	2,703	2,380	3,107	3,286

There were no surveys of new areas. The bulk of the resurvey work was carried out in Katsina, where 2,291 cases were found in 207,846 people examined

in five districts. The highest resurvey rates were in the Galadima (Mallamfashi) district, where 2·8 per cent. of 70,658 people proved to be infected. The rates in individual hamlets ranged from less than 2 per cent. to about 12 per cent. No clearings had been made in this district. In four other Katsina districts re-surveyed, the original infection-rates (1936–1937), compared with the present rates, were as follows : Kogo 9 per cent. : 0·1 per cent., Dan Ja 7 per cent. : 0·9 per cent., Musawa 1 per cent. : 0·1 per cent., and Kankara 11 per cent. : 0·9 per cent. Since the original surveys, in these districts, there had been no follow-up dispensary treatment as in other endemic areas, but clearance measures had been in operation.

In the more central endemic areas, in Zaria, Plateau, Niger and Bauchi Provinces, most routine re-surveys gave rates around 1 per cent. ; similar rates occur in Benue Province. More highly infected foci are known to exist, especially in Plateau and Bauchi.

The mines labour force controlled has fallen to about 4,500, scattered in at least 95 camps in 4 " restricted " areas. Examinations averaged at about 8 per man per year, yielding 227 infections, *i.e.* an index of new infections of 0·6 per cent. every 6 weeks, or about 5 per cent. per year. This is to be compared with incidences of less than 0·5 per cent. to 2 per cent., in surveys made at intervals of several years, in the surrounding peasant populations. There is no evidence of spread from the mining camps to the surrounding population.

Trials of pentamidine as a prophylactic were continued on a relatively small scale. The dose of isethionate now given is 200 or 250 mgm. intramuscularly. No statistics are provided in connexion with these trials. Large-scale trials planned for 1946 had to be abandoned, for lack of staff and of compulsory powers. The use of pentamidine is, however, now normal procedure in a number of Wamba camps, and it is given on engagement, and then every 4 or 5 months. It " obviously gives better results as a prophylactic than did antrypol in 1936 in the same area, but the infection rate is already so low from the regular six-weekly examination system that some time will have to elapse before conclusive figures are obtained."

The extent of communal protective clearance activities is described, province by province. An interesting point is mentioned in connexion with the troublesome feature of rapid regeneration from the stumps of the Tukuruwa palm (*Raphia vinifera*), common in streams south of Zaria, and infested with *G. palpalis*. It has been found that the laborious digging out of roots and stumps can be obviated by driving in a stake, but complete rotting can be ensured only by driving the stake into the true heart of the stump. A simpler, and even more efficient method, is to make a hole with a crowbar in the heart of each palm sucker, and to pour in a few ounces of cotton tar.

Further progress in the Anchau tsetse free corridor included 27 miles of new clearance and the sinking of 15 more well-shafts. Most of the other developments in the settlement were along the same lines as described in previous reports of recent years.

An appendix refers to drug trials. Investigation of *p*-arsenosophenylbutyric acid (also known as 70A, and " Butarsen ") [this *Bulletin*, 1945, v. 42, 15, 354, 970 ; v. 43, 1017] has been in progress since 1944. Early cases with no c.s.f. changes did well on this compound alone. Later cases responded badly, though they reacted favourably to " Butarsen " plus tryparsamide. This combination does not, however, appear to have been as efficacious as the standard synergic antrypol-tryparsamide course. Trials, still somewhat inconclusive, are also in progress with melarsen [this *Bulletin*, 1941, v. 38, 634], melarsen oxide [this *Bulletin*, 1946, v. 43, 207], mapharside, and with pentamidine isethionate. When given in higher dosages, the last-named compound has produced surprisingly good results even in cases with some evidence of

meningo-encephalitis. Intensive courses of pentamidine plus tryparsamide are therefore being compared with similar courses of antrypol plus tryparsamide.

E. M. Lourie.

Cookson, L. O. C. **The Serum-Formalin Reaction in *Trypanosoma rhodesiense* Sleeping Sickness.** *J. Trop. Med. & Hyg.* 1947, July, v. 50, No. 7, 134–40.

The organisms causing kala azar and trypanosomiasis are genetically and morphologically related ; presumably they also have antigenic affinities. There is excessive serum globulin and euglobulin production in the diseases caused by each, and this can be qualitatively estimated by the serum-formalin test. This test is easy to perform and to read, and it is suitable for field conditions. Its use in trypanosomiasis has been discussed previously [this *Bulletin*, 1925, v. 22, 539 ; 1926, v. 23, 427 & 894 ; 1927, v. 24, 958 ; 1938, v. 35, 705]. The cardinal signs of early sleeping sickness—fever, headache, debility, anaemia, lymphadenitis, C.N.S. symptoms, oedema, increased pulse rate, conjunctival infection, diarrhoea and wasting—may, any or all of them, be attributable to a variety of causes. The only proof of trypanosomal infection is the recovery of the causative organsims, and this is not always easy or practicable in the field.

The method of performance of the serum-formalin test, and its interpretation in terms of opacity and of gelification are detailed. Its value in the detection of cases of sleeping sickness was studied in five groups of persons. Group A consisted of 75 recruits for the N. Rhodesian Regt. from the tsetse-free areas—none gave a positive serum-formalin reaction. Group B consisted of 15 similar recruits from trypanosomiasis-endemic areas ; 6 of these gave weak positive reactions, though none was demonstrated to have an active infection (possibly a past infection may be the explanation). Group C was made up of 11 patients suffering from a variety of wasting illnesses, including open tuberculosis, but not trypanosomiasis ; in all but two the serum-formalin test was positive. Group D, 18 proven cases of *T. rhodesiense* infection, in all but one very early case, gave a positive reaction. Group E consisted of 8 persons suspected to be suffering from trypanosomiasis either on clinical grounds or because the serum-formalin test was positive. In all but one of these, the diagnosis was subsequently proved parasitologically to be correct ; in this exceptional patient, who absconded and died, the presumption was considerable.

The author accordingly concludes that the serum-formalin test affords information of great value in doubtful cases of trypanosomiasis and when the investigator is working under primitive conditions amongst a suspect population.

A. R. D. Adams.

Pellissier, Aimé. La tryparsamide dans la trypanosomiase nerveuse. Échecs et dangers de traitements insuffisants. Quelques réflexions sur arséno-résistance. [**Tryparsamide in Second Stage Sleeping Sickness. The Disadvantages of Insufficient Treatment, and Observations on Arseno-Resistance.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 9/10, 396–404 & 1947, v. 40, Nos. 1/2, 23–49. [77 refs.]

This is an excellent, if somewhat discursive, treatise. It is well supported by references to, and extracts from, published work, and includes a very useful exposition, together with the author's own evaluation, of views reached by various workers, especially French and Belgian, on the treatment of *gambiense* sleeping sickness up to March 1945. Due consideration is also given to the lessons of strictly laboratory researches, such as those on arsenic-resistance by Warrington Yorke and his co-workers.

Difficulties of supply in French Equatorial Africa, from June 1940, imposed the necessity of limiting treatment with arsenicals, in a high proportion of patients, to no more than six injections per case. Some four years after the beginning of this stringency, in the course of re-surveys especially in the Mayama-Brazzaville Sector, the author was struck by the high proportion of cases of nervous involvement. The belief that these were due to inadequate treatment impelled him to study the history of the use of tryparsamide, in general as well as in particular regard to the records of the Pasteur Institute at Brazzaville.

The earliest reports on the clinical use of tryparsamide gave particularly low success-rates [criteria of " success " undefined] in cases of nervous involvement, but as knowledge was acquired of the best way to use the drug, these rates gradually improved, as follows: 45 per cent., VAN DEN BRANDEN and VAN HOOF [this *Bulletin*, 1924, v. 21, 376]; 43 per cent., LAIGRET [this *Bulletin*, 1926, v. 23, 900]; 62·5 per cent., LEDENTU [this *Bulletin*, 1928, v. 25, 337]; 78·6 per cent., SICÉ [1928, *Arch. Inst. Pasteur de Brazzaville*]. In first stage cases, however, the results deteriorated so that the earliest success-rates of 100 per cent. gave way to 81·5 per cent. by 1927. Several writers accordingly reached the conclusion that while tryparsamide is the drug of choice in cases of nervous involvement, 270 Fourneau (Orsanine) is preferable in the lymphatico-blood stage.

By 1928 the Pasteur Institute, Brazzaville, had arrived at the basic principles, which continued to prevail until the time of writing, for the use of tryparsamide in second stage sleeping sickness. Weekly doses are slowly increased, from about 20 mgm./kilo, till the 3rd–5th injection, when a dose of 40 mgm./kilo for adults (50 mgm./kilo for children) is reached. This is continued to a total of at least 400 mgm./kilo for an adult, so that the course consists of about a dozen doses aggregating 22–25 gm. Higher individual doses, such as 60 mgm./kilo for adults and 90 mgm./kilo for children tested by CHESTERMAN [this *Bulletin*, 1932, v. 29, 638] do not improve the cure-rate, whilst they considerably increase the incidence of ocular damage. It is thought that replacing the first few injections of tryparsamide by two or three injections of Orsanine or Moranyl gives greater security against persistence of " lymphatico-blood " infection.

Although results with tryparsamide at the Brazzaville Institute gradually improved from 1924 to 1930, they have since become less satisfactory. In 1929 and 1930, the success-rates in cases of nervous involvement were 82 per cent. and 86 per cent., respectively. In 1936–1937 they were about 49 per cent., and for the next 6 years about 53 to 60 per cent. These are based on short periods of observation. Presumptive cures, *i.e.* after observation periods of several years were, at the time of writing, only about 45 to 50 per cent.

The records of the Mayama-Brazzaville sector during 1940–45 also gave a short-term success-rate of 60 per cent. in second stage sleeping sickness treated with full courses of tryparsamide. However, in 24 cases where the treatment was limited to 6 doses, there were only 37·5 per cent. short-term successes. This is similar to the results obtained among such cases as were treated with only 6 doses of tryparsamide in 1924–25. The conclusion is, therefore, that a course of 6 doses has consistently been less effective than one of 12 doses. Of 18 fully-treated patients lumbar-punctured after both the 6th and the 12th dose, 7 were found to present a deterioration in the c.s.f. picture half-way through the tryparsamide course, followed by a normal or subnormal picture at the end of treatment. [The reviewer (this *Bulletin*, 1943, v. 40, 370) also showed an increase, followed by a decrease to less than the original count, in c.s.f. cells in a fair proportion of Sierra Leone cases punctured both 5–6½ weeks and 4–5 months after the start of treatment with tryparsamide. The tendency towards such a

" hump ", at this early stage in the progress of the c.s.f. towards normality during successful treatment, may be misleading to those attempting to use early lumbar-puncture findings in order to assess the results of any particular treatment.] The author postulates that the meningeal reaction, apparently stimulated by the earlier part of the treatment-course, provides a favourable nidus for the further development of such trypanosomes as have thus far escaped the effects of treatment, and it is, therefore, especially necessary to complete the full course of 12 injections.

SALEUN (*Rapport Inst. Pasteur Brazzaville*, 1937) distinguishes three phases of second stage sleeping sickness : (1) congestive, when the parasites multiply in the meningeal vessels. This is the period of " meningeal reaction ", characterized by increase of leucocytes and no, or very slight, increase of albumin in the c.s.f. It is particularly responsive to Orsanine, and is followed by (2) the meningo-encephalitic phase, with great increase both of leucocytes and of albumin, together with the appearance of trypansomes in the c.s.f., and, finally (3) a phase of considerable parenchymatous damage to the central nervous system ; trypanosomes are able to shelter from the effects of treatment in the lesions produced at this period, and are thence able to invade other areas after treatment has stopped.

The author reviews evidence for " trypanotoxins ", and then discusses the mode of action of tryparsamide. This is subject to four main complicating factors, each of which is considered at great length. They are as follows :—

(1) *The neurotoxic action of tryparsamide.*—Optic nerve damage and arsenical polyneuritis are discussed in detail. An arsenical " meningitis " sometimes occurs, causing an increase in cells and albumin, particularly the latter. This has led some authorities to defer post-treatment lumbar puncture until 1–3 months after the injection-course. The author condemns this as a dangerous practice. He advises lumbar puncture 7 days after the end of treatment ; if the c.s.f. is normal the patient then reports every three months, otherwise he should be punctured again the following month. If on this occasion the fluid is normal, the previous result may be ascribed to a toxic meningeal reaction, and the patient is then placed on three-monthly observation ; if the fluid has hardly changed, the infection is regarded as not yet eradicated, and another course is administered ; and if the fluid has deteriorated then a relapse is registered, and this also, of course, necessitates further treatment.

Reference is made to "*l'hyperalbuminose cicatricielle*" (BRODEN and RODHAIN's phrase), an obstinate albumin-level at about 30 mgm. per cent., occasionally persisting for years in cured cases.

(2) *The action of " trypanotoxins ".*—The most notable effect under this heading is the Jarisch-Herxheimer reaction. The deterioration in the c.s.f. picture, mentioned above as sometimes occurring half-way through a full course of tryparsamide injections, is also placed under this heading, instead of being ascribed to an arsenical " meningitis ". Reasons for this conclusion are that the c.s.f. picture improves if treatment be continued to the end of the course, and it involves mainly an increased cell-count, whereas an arsenical " meningitis " is shown mainly by increased albumin.

(3) *Arseno-resistance of the trypanosome.*—An outline is given of the researches of Warrington YORKE and his co-workers, and the confirmatory work of others, on acquired resistance in trypanosomes. The author has little doubt, in view especially of reports from the Belgian Congo, that arseno-resistant strains of *T. gambiense* have arisen consequent upon previous treatment with arsenicals.

(4) *Arseno-resistance of the patient.*—Failure to respond to treatment may be due, not to arseno-resistance on the part of the trypanosome, but to inability

of the patient to utilize the arsenical adequately. In the course of a very long discussion under this head, the author stresses the importance of selecting the right arsenical for the particular stage of infection to be treated. He quotes, for example, a case in which he believes an unsatisfactory response to treatment to have been due to the fact that the lymphatico-blood stage was treated with tryparsamide instead of atoxyl or orsanine, either of the latter being regarded as more effective at that stage.

The author cites VAN HOOF *et al.* [this *Bulletin*, 1938, v. 35, 698] as to the decreased transmissibility by *Glossina* of trypanosomes from arseno-resistant patients, and he therefore interprets the trends of success and failure, in the Brazzaville Institute records since 1924 as follows: 1924–1930: increasing success, with increasing understanding of how to use tryparsamide. 1930–1937: fewer successes, due to appearance of arseno-resistance. After 1937: trend towards a plateau in the success-rate curve, due to the gradual establishment of an equilibrium between the tendency to an increasing number of cases of arseno-resistance on the one hand, and diminished transmissibility of trypanosomes from such cases on the other. He considers that the probable stabilization of this equilibirium obviates the danger, for the future, of considerable increases in the incidence of arseno-resistance. *E. M. Lourie.*

FOWLER, A. F. **Intensive Tryparsamide Therapy in the Treatment of Trypanosomiasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 763–70.

In general hospital practice in the Gold Coast it is customary to attempt to treat trypanosomiasis by 12 injections of tryparsamide, at intervals of one week. Tryparsamide is used because in most cases the central nervous system is already involved, and the patients attend as out-patients. Under these conditions the course is rarely completed, and the author therefore attempted intensive treatment so as to ensure, at least, that the patients actually received the intended amount of the drug.

Two methods were tried. The first consisted of intravenous drip infusion of about 2 gm. tryparsamide (for an adult) in 2 pints of double distilled sterile water, at the rate of 40 drops each minute; this takes about 8 hours. It was repeated each day (unless suspended for a time on account of pyrexia) for 6–9 days. The patient's arm was immobilized on a splint during administration. Pyrexia was common, and sometimes dangerous; it was ascribed to pyrogenic material in the solution, which could not be avoided under the circumstances.

The second method is not described completely, but apparently consisted of daily intravenous injections of [probably] 2 gm. tryparsamide in 10 cc. distilled water, presumably for 6–9 days. The author suggests that 14–16 gm. of tryparsamide are probably adequate for an adult weighing about 50 kgm.

In 72 patients treated by the first method, all of whom were diagnosed by one or more of the recognized methods, and of whom 56 showed involvement of the central nervous system, there were 11 deaths in hospital (in patients in poor condition), visual disturbance in 8, but a considerable immediate improvement in most cases. Of 39 followed up from 2 to 24 months, 32 were apparently cured.

In 13 patients treated by the second method, all of whom showed central nervous system involvement, there were no deaths, one had optic neuritis, all were improved, and 3 seen 10 months later were apparently cured.

The author admits that the numbers are too small for firm conclusions to be drawn. *Charles Wilcocks.*

VAN HOOF, L., HENRARD, C. & PEEL, E. Chimioprophylaxie de la maladie du sommeil par la pentamidine. [**Chemoprophylaxis of Sleeping Sickness by Pentamidine.**] *Ann. Soc. Belge de Méd. Trop.* 1946, Dec. 31, v. 26, No. 4, 371–84.

In the authors' original examination of pentamidine as a prophylactic agent against *T. gambiense* infection, guineapigs and human volunteers were protected for many months from the effects of repeated bites by infective tsetse flies. These results led them to successful trials of prophylaxis by pentamidine as a large-scale means of trypanosomiasis control in the field [this *Bulletin*, 1944, v. 41, 928; 1946, v. 43, 536].

It was pointed out by FULTON [this *Bulletin*, 1944, v. 41, 929] that the protective effect obtained in the above experiments in guineapigs might, in large measure, be attributable to an immunizing effect consequent on the repeated test-inoculations, quite apart from any prophylaxis conferred by the pentamidine itself. Similar considerations had been advanced by DUKE [this *Bulletin*, 1936, v. 33, 657] in connexion with the protection observed in volunteers treated prophylactically with Bayer 205, and the authors themselves had then examined the matter in guineapigs, but without being able to bring particularly strong support to Duke's conclusions [this *Bulletin*, 1940, v. 37, 703].

In view of the fact that the authors' recent work was done with different strains of trypanosome and different host species from those of other investigators, they decided to re-examine the question under circumstances which would eliminate the factor of immunization.

Experiments in guineapigs.—Each animal was subjected to only one, and not to repeated, attempts at inducing infection. The experiments led to the conclusion that complete protection against being infected with *T. gambiense* by the bite of infective tsetse flies is conferred for about 27 days by a single injection of 3 mgm./kgm., and for about 60 days by 3 injections of 2 mgm./kgm. on alternate days (dihydrochloride used; route of injection not stated). Beyond these periods, guineapigs become infected, but with prolonged incubation periods and with very irregular parasitaemia, this relative degree of protection sometimes extending for even as long as 6 to 10 months. The duration of absolute protection appears to be slightly shorter—53 days after 3 injections of 2 mgm./kgm. pentamidine—when tested by inoculation of trypansomes instead of by bite of infected tsetse flies.

Protection could not be augmented by repeated injections of rich and live cultures of *T. gambinese* at intervals after the prophylactic dose of pentamidine.

The protection periods, in the absence of any immunizing factor, were therefore appreciably longer than those obtained by FULTON with *T. rhodesiense* in mice, thus suggesting that parasite-species and host-species are important factors in this connexion.

Experiments in man.—Three human volunteers were given intramuscular injections of 4·5 mgm./kgm. of the di-isethionate. They were then bitten by infective tsetse flies after periods, respectively, of 48–53, 90–92, and 184–5 days. All three patients failed to become infected. The tsetse flies were proved to be infective by later applying them to guineapigs, and by dissection.

The authors therefore conclude, though themselves admitting the evidence to be scanty, that pentamidine *can guarantee* the African against natural infection for a period of 6 months [their own italics]. They point out the administrative advantages of a drug which can exercise such a property. The period of protection conferred by Bayer 205 is considered to last no longer than 3 months, and toxic complications are more likely after intravenous Bayer 205 than after intramuscular pentamidine di-isethionate.

Since 1943, large-scale trials of prophylactic pentamidine, mainly at a dose of 5 mgm./kgm., have been in progress in the Belgian Congo, and results will be published in due course. *E. M. Lourie.*

LEWIS, E. A. & LANGRIDGE, W. P. **Developmental Forms of *Trypanosoma brucei* in the 'Saliva' of *Glossina pallidipes* and *Glossina austeni*.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 6–13, 1 pl. & 35 figs. [13 refs.]

These observations of the developmental forms of *Trypanosoma brucei* in two species of tsetse flies—*Glossina pallidipes* and *G. austeni*—were made by examining under the microscope stained fixed smears of the fluid ejected from the proboscis of the fly on to warm glass slides, the technique recently described by BURTT [this *Bulletin*, 1946, v. 43, 1121] being used. The laboratory-bred flies were fed on an animal infected with a strain of *T. brucei* that was isolated from a camel in 1944 and afterwards maintained by direct and cyclical transmissions through a variety of vertebrates. About the 14th day after the first feed, the flies were starved for 48 hours and induced to eject fluid from the proboscis on to the slides and were fed immediately afterwards; this procedure was repeated every 48 hours, and from the examination of these slides the authors deduced the course of morphological development of the trypanosomes in the flies from the stages found in the proventriculus to the infective forms in the salivary glands.

They observed trypanosomes and crithidia of various shapes and sizes such as have been described in previous accounts of the development of the polymorphic trypanosomes in other species of tsetse flies, references to which are given in the paper. The first form to appear in the slides was the typical proventricular trypanosome; tadpole-like trypanosomes (called by the authors post-proventicular forms), crithidia and metacyclic trypanosomes appeared later, but as development proceeded the flagellates in the smears became very numerous, making observation more difficult.

The course of development from the proventricular trypanosome to the final metacyclic trypanosome is thought by the authors to be as follows: the cytoplasm of the typical proventricular trypanosome flows into its posterior part producing a somewhat tadpole-like appearance, the anterior part becoming attenuated; this is called a "post-proventricular" trypanosome. The nucleus becomes elongated, passes into the posterior swollen part, and divides into two, this division being preceded by division of the kinetoplast. Each daughter kinetoplast lies close to and in front of a corresponding daughter nucleus and the cytoplasm splits to form two crithidia—a short aflagellate one cut off as a section of the swollen posterior end and a long flagellated one. The latter probably degenerates while the former develops a flagellum, migrates to the salivary gland and becomes attached there by its flagellar end. It divides nearly equally by fission and the posterior half develops a flagellum and separates off as a free crithidia which becomes a metacyclic trypanosome; this is broad at first but becomes thinner later. The authors give dimensions of these various forms.

Coiled-up and round forms appeared several days later than the metacyclic trypanosomes; as they were rarely seen before the flies showed signs of debility, the authors regard them as arising only in adverse circumstances and not as part of normal development.

Short crithidia were regularly present in smears from all flies which became infective and were rare or absent in smears from flies which failed to transmit the infection.

The authors' strain of *T. brucei* developed more readily and produced daughter crithidia more frequently in *G. pallidipes* than in *G. austeni* under similar conditions. [Must there not be some doubt about the places of origin of some of the crithidia and trypanosomes seen in the smears ?] *J. F. Corson.*

Vaisman, A. L'atténuation de l'infection trypanosomique expérimentale chez la souris, par le *Spirocheta duttoni*. [**Attenuation of Experimental Trypanosomiasis in Mice by** *Spirochaeta duttoni*.] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 74–6.

The author studied the effect on mice experimentally infected with *Trypanosoma equiperdum* and *T. brucei* of injecting quantities of *Trep. duttoni*. In common with previous workers they had already noted that the presence of *Trep. duttoni* in the blood of such mice had delayed the appearance of trypanosomes.

All infections were produced by intraperitoneal injection. The experiments consisted of injecting the spirochaetes (1) simultaneously with the trypanosomes, (2) 2 to 8 days before the trypanosomes, (3) 24 hours after. In (1) both parasites appeared in the blood on the second day ; the trypanosomes, instead of killing the mice within the week, disappeared from the circulation in 4 to 5 days ; the spirochaetal infection pursued its usual course. After a variable period of 15 to 40 days, the trypanosomes reappeared and usually killed the mice in a few days. In two cases, however, complete recovery occurred.

In (2) the first appearance of the trypanosomes was delayed and, in general, their numbers were not very high during the acute stage of the spirochaetal infection ; otherwise the course was identical with that of (1). In (3) the action was the same as (1).

Exceeding the time limits of 8 days in (2) and 24 hours in (3) interfered with the phenomenon, producing either a slightly delayed action or increased virulence respectively.

The effect of the spirochaetal infection on the trypanosomiasis occurred only in the acute stage of the former.

Further experiments, which are described, suggested that this attenuating effect could not be accounted for either by a direct action of *Trep. duttoni* on the trypanosomes or by the development of trypanocidal antibodies in the surviving mice.

The trypanosomes which reappeared in the relapses did not develop any resistance to further spirochaetal infection. *H. J. O'D. Burke-Gaffney.*

LEISHMANIASIS.

i. de Azevedo, J. F. Novos dados sobre a biologia das espécies de *Phlebotomus* de Lisboa e arredores. [**New Biological Data concerning the** *Phlebotomus* **Species in Lisbon.**] *An. Inst. Med. Trop.* Lisbon. 1946, Dec., v. 3, 7–20, 3 figs. (2 on 1 pl.). English summary.

ii. —— & Teixeira, A. W. G. Sobre as preferências hemáticas das espécies portuguesas de *Phlebotomus*. [**Blood Preferences of Portuguese Species of** *Phlebotomus*.] *Ibid.* 159–81. English summary.

iii. ——. Uma anomalia rara verificada numa fêmea de *Phlebotomus perniciosus*. [**A Rare Anomaly in Female** *Phlebotomus perniciosus*.] *Ibid.* 183–6, 3 figs. (2 on pl.). English summary.

i. In the first paper the author gives the results of a *Phlebotomus* survey in and around Lisbon. The following species were captured, but only between

May and November; *P. perniciosus* (most common), *minutus*, *sergenti*, and *ariasi*. The resting places in order of preference were, cattle-sheds, pig-styes, human dwellings, stables, fowl-pens, dog-kennels and rabbit-hutches. The blood preferences were chiefly bovine and then dog, fowl, horse, man and pig. Among 2,614 *Phlebotomus* dissected only one specimen (*P. perniciosus*) was found infected by a form of leptomonas, of which photographs are given for comparison with photographs of leptomonas forms from a culture of *Leishmania donovani*.

ii. The authors of the second paper describe the technique of the precipitin tests performed on the blood contained in the alimentary tracts of the 2,614 *Phlebotomus* mentioned in the first paper. They analyse in greater detail the results of the tests. Of 603 reactions, 22·5 per cent. were positive with anti-bovine serum, 1 per cent. with anti-canine, 3·3 per cent. with anti-horse, 2·3 per cent. with anti-bird, 1 per cent. with anti-pig and 2 per cent. with anti-human.

iii. In the third paper the author describes, and illustrates by photographs and drawings, a specimen of *P. perniciosus* with three spermathecae. It was found among 5,736 females caught during the above survey. *H. S. Leeson.*

DOLMATOVA, A. V. [**On the Biology of Sandflies inhabiting Burrows.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946 [1947], v. 15, No. 6, 47–55, 3 figs. [In Russian.]

In view of the epidemiological importance of sandflies inhabiting burrows of wild animals which serve as reservoir hosts of human leishmaniasis, the author undertook a study of the biology of these insects at Shulavery in the Georgian Republic, Caucasus. The observations were carried out during the summer of 1945 in a ravine containing numerous burrows, some of which were occupied by nesting birds. The sandflies were caught on adhesive paper and in gauze traps set at the entrance to the burrows. The local sandflies comprise the following eight species: *Phlebotomus papatasi*, *P. sergenti*, *P. perniciosus* var. *tobbi*, *P. chinensis*, *P. kandelakii*, *P. perfilievi*, var. *transcaucasicus*, *P. sergenti* var. *mongolensis*, *P. minutus* var. *arpaklensis*. All of these forms were recovered from burrows, but only five (*P. papatasi*, *P. perniciosus* var. *tobbi*, *P. sergenti*, *P. chinensis* and *P. kandelakii*) were found in houses.

The flight of sandflies into and out of the burrows always took place during the evening hours, the stimulus for their emergence probably being the onset of twilight rather than difference in temperature and humidity. The majority of sandflies flying out of the burrows were hungry individuals, including both new-born females and those which had laid eggs, but the majority were males. The number of sandflies leaving inhabited burrows was 5–6 times greater than that emerging from uninhabited ones. In the former case the sandflies contained food in all stages of digestion, except the 2nd and 3rd stages. In the latter case the majority (81 per cent.) were hungry individuals, which included females which had laid eggs, from which it is evident that the burrows serve as breeding places for these insects.

The author notes that cases of leishmaniasis occur in the district in question, and considers the relative epidemiological importance of the burrow sandflies in the transmission of the disease. It is thought that *P. minutus* var. *arpaklensis* is of no importance since its females do not occur in houses and it has not been seen to attack man in the open. On the other hand, *P. perniciosus* var. *tobbi* is abundant in burrows, constitutes 22·7 per cent. of the species found in houses, and attacks human beings in the open. Since it can be infected with *L. donovani* under experimental conditions, it is conceivable that this species might serve as a natural vector of the infection. As regards *P. sergenti*, although it readily

attacks man, its numbers both in the burrows and in houses are too small for it to be of much importance in the transmission of leishmaniasis.

C. A. Hoare.

ADLER, S. **The Behaviour of a Sudan Strain of** *Leishmania donovani* **in** *Phlebotomus papatasii*. **A Comparison of Strains of Leishmania.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 701–12, 2 figs. on 1 pl. [15 refs.]

The behaviour in *P. papatasi* of a Sudan strain of *Leishmania donovani* was studied. Flies became infected after feeds on (*a*) cultures; (*b*) infected spleens; and (*c*) hamsters suffering from the disease. In the case of (*a*), the infection tended to die out in a few days. None of these flies was able to transmit leishmaniasis by bite, but inoculation of the contents of the mid-guts was followed by infection. Only 2 out of 51 of the sandflies feeding on infected hamsters became infected, and then only in the stomach; this phenomenon provides one method of distinguishing strains, different strains giving significantly different infection rates in various species of *Phlebotomus*. It is assumed that when infection is low, there is an active natural immunity in the fly against a certain species, though the immunity may be broken down by employing massive doses of parasites.

The author then proceeds to show how the various species may be differentiated:—

L. tropica.—In Syrian hamsters, visceral and skin infections are produced, the parasites measuring as much as $5{\cdot}6\mu \times 3\mu$. Culture on Locke-serum-agar produces thick granular masses of flagellates. High infection rate in *P. papatasi*.

L. infantum.—In Syrian hamsters, visceral and skin infections are also produced, but the parasites seldom measure more than $4{\cdot}2\mu \times 2{\cdot}8\mu$. Culture produces uniform character of growth. [The plate (Fig. 1) is misnamed "*donovani*"; Prof. Adler has pointed out to the reviewer that it should read "*infantum*".] Low infection rate in *P. papatasi*, but parasites progress anteriorly.

L. donovani.—In Syrian hamsters, visceral and skin infections (with small parasites). Growth of Indian strains in culture is rather thicker than in *infantum*. Low infection rate in *P. papatasi*, parasites mainly confined to stomach.

L. brasiliensis.—In Syrian hamsters, local infections only.

There are discrepancies in the behaviour of local strains which have led the author to suppose that mutation had occurred. *P. C. C. Garnham.*

ADLER, S. **Cellular Reactions in Leishmaniasis.** *Acta Med. Orientalia.* 1947, May, v. 6, No. 5, 151–5, 4 figs.

The characteristic reaction in leishmaniasis of mammals is proliferation and parasitization of the cells of the reticulo-endothelial system. There is also a secondary reaction, a round-cell infiltration, and this is usually associated with a marked reduction in the number of leishmania in the tissues thus infiltrated. The author believes that this second reaction is a curative one. He points out that in the spermophil, in which experimental infection with *Leishmania donovani* is invariably fatal (the animal dying in two to four months), there is an intense proliferation of the reticulum cells with little evidence of round-cell infiltration. On the other hand, in the dog in which the infection is nearly always subacute and often symptomless, the proliferation of the reticulum is accompanied by round-cell and plasma-cell infiltration. The author also points out that in experimental *Leishmania tropica* infection of man, in the

early stages, a syncytium of parasitized reticulum cells is formed with no round cells, and that this is followed by an intense round-cell reaction with a continuous diminution of the leishmania.

He concludes that lymphocytes appear to play some part in the defence mechanism against leishmania infection. *L. E. Napier.*

DE AZEVEDO, J. F. Diagnostic du kala-azar méditerranéen par la recherche des leishmania dans la muqueuse nasale. [**Diagnosis of Mediterranean Kala Azar by Examination of the Nasal Mucosa.**] *Arch. Inst. Pasteur d'Algérie.* 1947, Mar., v. 25, No. 1, 52–61, 1 fig. [10 refs.]

For the definite diagnosis of kala azar, it is necessary to demonstrate the causal parasite, *Leishmania donovani*. Although there are many other diagnostic procedures, none is entirely specific. The parasite has been found in the material drawn from the spleen, the liver, the lymphatic glands and the skin ; it has been found in the bone marrow, blood, faeces, urine, saliva and sputum, and in scrapings from the nasal mucosa.

Spleen puncture is the most certain method, usually giving 100 per cent. positive results, but it is not entirely without danger and requires a delicate technique. Sternal puncture gives a lower percentage of positive results (about 87 per cent.), as does liver puncture also. Gland puncture is difficult, since the glands are seldom sufficiently enlarged, and in Mediterranean kala azar parasites are found in the blood in only 1 per cent. of cases. The findings of parasites in the faeces, urine, saliva and sputum are of epidemiological significance, but cannot be considered practical diagnostic procedures.

Investigators in different countries have found *L. donovani* in the nasal mucosa—FORKNER and ZIA [this *Bulletin*, 1934, v. 31, 656] in China (54·5 per cent.) ; SHORTT and SWAMINATH [this *Bulletin*, 1936, v. 33, 16] in Assam (40·0 per cent.) ; HENDERSON [this *Bulletin*, 1938, v. 35, 178] in the Sudan (7·5 per cent.) ; and FRAGO DE AZEVEDO (the author) in Portugal (8·18 per cent.). The author considers that in the Mediterranean zone this is a practical method of diagnosis.

He uses an ordinary platinum loop, a curette, or a needle. He scrapes the nasal mucosa at various points, preferably where it is thick. It is not necessary to use a speculum. When some blood appears on the platinum loop, this is smeared on to a slide and stained with Leishman's stain. As the parasites are in the histiocytes in the submucosa, it is necessary to break the surface ; a superficial smear is useless. It is not necessary to use a local anaesthetic ; no discomfort follows, but occasionally there is a little epistaxis.

He obtained positive results in 9 out of 11 cases by this method. In one of the negative cases, five examinations of the mucosa were made ; the sternal puncture was also negative but the spleen puncture positive. In the other, only one mucosal examination was made ; the spleen puncture was positive.

The advantages of this method are its simplicity and safety ; it can be carried out in all cases even before the spleen is enlarged, and it can be used to check progress under treatment. *L. E. Napier.*

FALCÓN TREJO, A. Algunas historias de kala-azar infantil. [**Some Cases of Infantile Kala Azar.**] *Med. Colonial.* Madrid. 1947, Apr. 1, v. 9, No. 4, 322–5.

Infant kala azar is more common in Badajoz than is generally believed because cases are at times by no means typical. The author gives details of three such atypical cases. In two (sisters) there was fever, but in the early stage in one no enlargement of spleen nor positive serological reactions, but cervical adenitis with some degree of anaemia and relative lymphocytosis. In the

second, the symptoms were similar but, when the child was seen two months later, the serological reactions were positive. A third child had daily fever, sometimes with shivering, diarrhoea, and a spleen palpable on deep inspiration. Intestinal infection was considered, but the Nattan-Larrier reaction [this *Bulletin*, 1936, v. 33, 21] was positive and the conditions cleared up on administration of neostibosan. Two other cases are recorded in which kala azar was suspected because of fever, anaemia and relative lymphocytosis, but in one the cause was malaria and in the other *Salm. typhi*, serum reactions for kala azar being negative. No mention is made of puncture of spleen or sternum, except to say that in the country districts these are difficult, if not impossible, to carry out. *H. Harold Scott.*

DEBONO, J. E. **Kala-Azar in Infancy.** *Proc. Roy. Soc. Med.* 1947, Feb., v. 40, No. 4, 155–59 (Sect. of Paediatrics 1–5), 1 fig.

The paper is a description of kala azar as seen in Malta. There is no essential difference between infantile and adult kala azar. The disease is, in any case, not confined to infants, but rather to young children. In 200 cases, the numbers in each of the first 8 years of life were 10, 76, 55, 26, 20, 8, 2 and 3, respectively: that is, 97·5 per cent. were under the age of 6. None was over 8 years.

The basic pathological lesion is an invasion by leishmania with resultant proliferation of the reticulo-endothelial tissues in all parts of the body, the spleen and liver being mostly affected. There is hypochromic anaemia (2·5 million red cells) and marked leucopenia (2,000 or less), with granulopenia and absolute as well as relative monocytosis.

The incubation period is usually 3 to 4 months, but may be much longer. The onset is usually insidious with irregular pyrexia, loss of appetite and energy, weight and colour; the fever subsides after 2 to 6 weeks; there is a remission of similar length; and this is followed by another febrile bout. The spleen enlarges progressively at the rate of about 2 fingers breadth per month. The fever continues and there may be alternating attacks of diarrhoea and bronchitis. However, the disease may take an acute course from the beginning, or hyperpyrexia, cyanosis and haemorrhages in the skin may develop and prove rapidly fatal.

Diagnosis in the early stages is difficult. The 4-hourly temperature chart usually shows a double or triple daily rise, and there is usually leucopenia: confirmation must be obtained by blood culture, since at this stage the spleen is too small to puncture. [Bone puncture is useful at this stage.] When the disease is well developed, diagnosis is easier, but many febrile conditions such as undulant fever must be excluded. Diagnosis is best confirmed by spleen puncture. The author has done 2,000 spleen punctures with only two deaths.

The disease responds well to treatment by intravenous antimony. Neostibosan was used before the war, but during the war Neostam only was available. The initial dose of 0·05 gm. is usually given and this is increased to the toleration limit, up to 0·3 gm. in children over 3 years of age. Sixteen injections are given on alternate days. The course is repeated if necessary after two months. Adjuvant treatment for obviating or eradicating secondary infections is important, and penicillin has been used for this purpose.

The author recorded 3 deaths and 7 relapses in a series of 200 cases. In reply to a question by Colonel SHORTT, he said that he had never seen an instance of dermal leishmanoid.

Colonel Shortt discussed the transmission of kala-azar. He said that, as dogs were the reservoirs of infection in the Mediterranean area and were very heavily infected, there was probably a very heavy sandfly infection here. He suggested

that the children who did not develop kala azar, for some reason or another, developed an immunity as a result of repeated bites from infected sandflies, and were thus protected from infection in later life. Local adult inhabitants are seldom affected, but visitors are affected quite frequently.

L. E. Napier.

MARPLE, C. D. **Visceral Leishmaniasis (Kala-Azar) : Report of a Case.** *Ann. Intern. Med.* 1947, May, v. 26, No. 5, 787–95, 2 charts & 1 fig.

A full description of a case in a white American who had served in India.

ECKER, H. D. & LUBITZ, J. M. **Kala-Azar in the United States : Review of the Literature and Report of Two Cases : Stilbamidine Treatment.** *Ann. Intern. Med.* 1947, May, v. 26, No. 5, 720–33, 6 figs. [41 refs.]

A review of 9 cases previously reported in the United States and a description of two new ones ; both of the patients had lived in Calcutta.

KIRK, R. **Studies in Leishmaniasis in the Anglo-Egyptian Sudan. VIII. Some Observations on the Chemotherapy of Kala-Azar.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Mar., v. 40, No. 4, 459–78. [63 refs.]

The author has outlined the advances made in the treatment of kala azar in the Sudan, where he has had a wide experience of this disease during the last 10 years. Rapid progress followed the use of antimony in the form of tartar emetic, which was introduced more than thirty years ago and was followed shortly afterwards by pentavalent organic compounds of this metal. It was some years later, however, before these compounds were used in the Sudan. Before the introduction of the new therapeutic agents, a fatal outcome of the disease was almost inevitable ; now, 70 per cent. of cures may be obtained in that country. Although this percentage of cures is lower than that recorded from India, it is undoubtedly evidence of a remarkable achievement, in view of the resistant nature of the disease in the Sudan, which requires about 3 times as much Sb for its successful treatment as does its counterpart in India. The patients seen by the author were often *in extremis* before offering themselves for treatment, partly on account of poor nutritional status and partly because of other intercurrent infections. Death commonly occurred in these patients soon after treatment was begun, because of the onset of pneumonia or diarrhoea. More attention was therefore devoted to hygiene and to the general well-being of the patient. As a result of appropriate measures, the death-rate in treated cases has fallen. While clinicians are not always agreed on the most suitable drug for treatment, the author thinks highly of neostibosan.

It is not clear whether the resistance to antimony shown by Sudanese cases depends on the parasite or the host. With the advent of the amidines, " resistant " cases proved more amenable to treatment and a higher rate of cure resulted. The question of cure may possibly be decided on clinical grounds, but the surest evidence is provided by absence of relapse over a period of 6 months or more. The author regards the appearance of dermal lesions during or after the treatment of Sudanese kala azar as being of good prognostic significance ; and it then appears to be associated with immunity to reinfection. While dermal lesions may persist for a period of 20 years or more without affecting health, they may nevertheless prove a source of infection for others. This fact should be borne in mind with regard to the after-care and disposal of affected patients.

J. D. Fulton.

See also p. 1012, BARTTER *et al.*, **The Fate of Radioactive Tartar Emetic administered to Human Subjects.**

Ho, E. A., Hsu, T. H. & Soong, T. H. **Canine Visceral Leishmaniasis in Villages West of Lanchow, China.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 889–94, 1 map. [13 refs.]

"Forty-four dogs naturally infected with visceral leishmaniasis were found among 1,430 examined in villages about 50 km. west of Lanchow. Epilation and seborrhoea were present in all but one of the dogs. Leishmania were found by skin biopsy in thirty-eight of the forty-four dogs and by ilium puncture in thirty-nine of forty-one dogs in which this operation was performed. The altitude of the area under study ranges from 5,656 to 7,788 feet above sea level. On this high plateau kala-azar, as well as sandflies, was also found to be present."

Dostrovsky, A. & Sagher, F. **The Intracutaneous Test in Cutaneous Leishmaniasis.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 265–9. [12 refs.]

It is often difficult, and sometimes impossible, to demonstrate leishmania in the cutaneous leishmaniasis (oriental sore) lesion. This is particularly true of the recurrent and other chronic types of lesion. Therefore some more reliable diagnostic procedure should prove useful. The use of leishmania vaccine for this purpose was suggested by Montenegro (1926) [this *Bulletin*, 1926, v. 23, 585], and in 1935, Dostrovsky [*ibid.*, 1936, v. 33, 21] demonstrated positive skin reactions by the intracutaneous injection of a vaccine containing 100,000 per 0·1 ml.

Both the intracutaneous test and the parasitic examination were carried out in 217 cases of leishmania nodosa in Jerusalem; the intracutaneous test was positive in 95·3 per cent. and parasites were demonstrated in 54·3 per cent. In 47 cases of recurrent leishmaniasis, the parasites were only demonstrated on 4 occasions, whereas the intradermal test was positive in all but one case. The chances of a non-specific reaction are low; in only 7 out of 94 control cases did a positive reaction occur, in five of these there was a possibility of a previous leishmaniasis lesion, and in two only was this possibility ruled out.

Two strains of vaccine were used, a Palestinian and a Baghdad strain, in 147 cases. No significant difference in the reaction was demonstrated.

To test the time of the first appearance of the reaction, 3 volunteers were inoculated with 2 million living leishmaniae; in two cases the reaction was positive on the second day after inoculation and in the third a slightly positive reaction was obtained on the 3rd and 13th days and a definitely positive reaction after 5 weeks. In one case of recurrent leishmaniasis the reaction was persistently negative until the lesion had healed under treatment with Grenz rays.

In 11 passive-transfer experiments, with serum from a patient with a recurrent leishmaniasis lesion, and from another with an old scar of 30 years' duration, four gave positive results. This suggests that antibodies develop which, after transfer to a non-immune subject, will give rise to a positive reaction. This appears to indicate that the reaction is an allergic one. *L. E. Napier.*

Steinhauer, L. **Recurrent Verrucous Leishmaniasis of the Skin (Oriental Sore).** *Acta Med. Orientalia.* 1947, Mar., v. 6, No. 3, 91–4, 2 figs.

A chronic dermal leishmaniasis lesion, which simulates lupus vulgaris and in which it is difficult to demonstrate leishmania except by cultural methods, is common in Palestine. It is usually described as "recurrent cutaneous leishmaniasis". The diagnosis is often difficult, but a tentative diagnosis

can be made by means of an intradermal leishmania-vaccine reaction, which is positive in 97 per cent. of cases. Biopsy shows a characteristic tuberculoid structure.

The author describes a verrucose form of recurrent cutaneous leishmaniasis. A patient had severe injuries to his hands ; after the hands had healed a small area (5 cm. in diameter) of infiltration, surrounded by a narrow zone of hyperaemia, appeared on the back of each hand, and spread. Later the verrucose infiltration became raised 1 cm. above the skin level. No diagnosis was made, but leishmaniasis was suspected on the grounds of a positive leishmania-vaccine test, and X-ray treatment was given. The patient was not seen for 3 years, during which time the lesions extended, involving the whole of the backs of both hands and appearing as raised warty masses. There was hyperkeratosis of the palms, and bluish papules on the forearms. Tuberculosis was excluded by histological section and guineapig inoculation. The diagnosis of leishmaniasis was confirmed by cultural methods. Treatment with Grenz-rays was given and considerable improvement effected.

This verrucose form of leishmaniasis, which is common in South America, is rare in the Middle East. *L. E. Napier.*

SALTZMAN, A. **Fluorophotometric Estimation of Stilbamidine in Urine and Blood.** *J. Biol. Chem.* 1947, May, v. 168, No. 2, 699–703, 2 figs.

Estimations of stilbamidine in biological fluids have been made by various authors, either by utilizing the vivid blue fluorescence which it emits in ultraviolet light, by formation of a coloured compound with glyoxal, or by spectrophotometric methods [this *Bulletin*, 1943, v. 40, 122 ; 1944, v. 41, 930 ; 1945, v. 42, 264 ; 1946, v. 43, 17]. In the method now described, solutions containing the substance, such as urine and plasma, were passed through an adsorbing column (Decalso) without previous removal of protein. Elution was then carried out by means of HCl-alcohol and estimation completed by comparison with suitable standards in a fluorophotometer with the use of suitable filters. The details must be consulted in the original. It was found that fluorescence deteriorated rapidly during measurement (a saturated non-fluorescent product is formed in light). The accurate measurement of 1 γ per cc. of fluid is claimed, with a recovery rate of 87 per cent. in trial samples.

[T. W. Goodwin in collaboration with the reviewer discarded the method of adsorption on Al_2O_3 followed by spectrographic estimation, because of the impossibility of eluting quantitatively the material added to urine in a sufficiently pure state. It is to be regretted that the term "Blood" in the title of this paper refers only to plasma.] *J. D. Fulton.*

FULTON, J. D. & DUNITZ, J. D. **Constitution of the Irradiation Product from Stilbamidine.** [Correspondence.] *Nature.* 1947, Aug. 2, 161–2, 2 figs.

FULTON and YORKE [this *Bulletin*, 1943, v. 40, 23] observed that stilbamidine underwent photochemical changes when its solutions were exposed to light and that a more toxic substance was produced. The nature of the irradiation product has been discussed by a number of workers [*ibid.*, 376, 684].

As far back as 1902, CIAMICIAN and SILBER (*Berichte deut. Chem. Gesellschaft*, 1902, v. 35, 4128) exposed a solution of stilbene in benzene to sunlight over a long period and isolated a hydrocarbon of m.p. 163° which by further experiments they considered to be a dimer of stilbene C_{28} H_{24}. The present authors have now prepared this substance by irradiating a similar solution with a mercury vapour lamp and have shown that the product of irradiation of stilbamidine is also a dimer, 1 : 2 : 3 : 4-tetra-(4′-amidinophenyl)-*cyclo*butane.

The toxic product formed was isolated, purified as the sulphate, and converted by hydrolysis to the corresponding tetra-acid ; on decarboxylation, this gave the hydrocarbon m.p. 163° mentioned above, together with a small quantity of another empirically similar hydrocarbon having an m.p. of 149°.

The characters and chemical structure of the two hydrocarbons and the investigational approach undertaken are discussed in detail and should be read in the original. *H. J. O'D. Burke-Gaffney.*

HENRY, A. J. **Fluorescence " Fatigue ".** [Correspondence.] *Nature.* 1947, Aug. 2, 163.

The author deprecates the use of the term fluorescence " fatigue " stated by ALPER (*Nature*, 1946, Sept. 28, 451) to be present in certain substances, such as vitamin A and riboflavin, on continued irradiation, on the ground that it suggests an analogy with the phenomena of elastic or muscular fatigue.

He discusses his own recent work on the photochemical instability of stilbamidine (*J. Chem. Soc.*, 1946, Dec., 1156) and considers that the changes in fluorescence which occur in solutions of these compounds on irradiation can be explained completely in terms of the photochemical change which occurs : a similar explanation may be found in the case of riboflavin, and this can be readily demonstrated by the method described by himself with GRINDLEY [this *Bulletin*, 1945, v. 42, 783].

" It is scarcely conceivable that any process at all comparable with either type of fatigue can occur in the case of a fluorescent molecule, particularly in dilute solution." *H. J. O'D. Burke-Gaffney.*

FEVERS OF THE TYPHUS GROUP.

DAVIS, W. A. **Typhus at Belsen. I. Control of the Typhus Epidemic.** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 66–83, 1 fig.

The author's earlier report on typhus at Belsen had a restricted circulation and so was not generally available ; it was reviewed in this *Bulletin*, 1946, v. 43, 427, and as the present report covers the same ground no further abstract is called for. *John W. D. Megaw.*

SNYDER, J. C. **Typhus Fever in the Second World War.** Reprinted from *California Med.* 1947, Jan., v. 66, No. 1, 30 pp. [69 refs.]

CHATTERJEE, P. K. & BANERJEE, A. **Typhus Fever in Calcutta.** *J. Indian Med. Ass.* 1947, Feb., v. 16, No. 5, 157–8.

Account of a case of scrub typhus in a patient who had not left Calcutta for a month previously.

PHILIP, C. B. **Observations on Tsutsugamushi Disease (Mite-borne or Scrub Typhus) in Northwest Honshu Island, Japan, in the Fall of 1945. I. Epidemiological and Ecological Data.** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 45–59, 8 figs. [24 refs.]

The author states that in 1893 Kitasato gave serious credence to the early beliefs of Japanese farmers that " flood fever " was caused by the bites of mites which were known locally as aka-mushi (red mites) and tsutsuga-mushi (dangerous mites) ; he mentions that in the same year SMITH and KILBOURNE made the historic discovery of the transmission of cattle fever by a tick.

The paper contains interesting observations made by the author during a visit in October 1945, to two of the three known areas of endemicity of tsutsugamushi disease in Honshu Island. The incidence of the disease has greatly diminished during the past 10 years from about 200 to 250 cases yearly to 43 in 1943 and 38 in 1944. The case-fatality rate remains high (36 deaths among 81 cases in 1943–44), and no evidence could be found of the occurrence of mild undetected attacks.

Complement-fixation tests were carried out on sera of four persons convalescent from attacks in 1944 and of three persons attacked in 1945. Using the Karp (New Guinea) antigen the titres observed in the former group were 1–64 ; 0 ; 1–8 ; and 1–4 ; with the Gilliam (Burma) antigen the titres were 1–512 ; 1–32 ; 1–32 ; and 1–4 respectively.

With the same strains of antigen in testing persons attacked in 1945 the results were : with Karp antigen 1–32 ; 1–512 ; and 1–512 ; with Gilliam antigen all three were negative.

These findings show the need for caution in interpeting the results of the complement-fixation tests.

Reasons are given for regarding the name *Rickettsia tsutsugamushi* Hayashi as having precedence over *R. orientalis* Nagayo *et al.* The evidence is, however, somewhat confusing and ambiguous ; Nagayo is admitted to have been the first (in 1924) to recognize the true nature of the causal agent, and those interested must read the discussion in the original paper.

In Nügata, the more heavily infected of the two areas, five species of larval mites were found on the field vole (*Microtus montebelloi*) ; they were *Trombicula akamushi*, *T. pallida*, *T. palpalis*, *T. japonica*, and a new species of *Gahrliepia*. In the other area, Yamagata, a small mouse-like rat, *Apodemus speciosus*, was found harbouring all the above mites except *T. akamushi*.

No mites were found in the nests of either of the above rodents.

John W. D. Megaw.

Philip, C. B. **Observations on Tsutsugamushi Disease (Mite-borne or Scrub Typhus) in Northwest Honshu Island, Japan, in the Fall of 1945. II. Systematic Comment on the Japanese Vole-Mites.** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 60–65. [21 refs.]

The author, without claiming finality, offers comments on the very confusing subject of the nomenclature of the various mites described by Japanese workers as occurring on field voles. He gives a key to the identification of the known species.

The paper is highly technical and must be read in the original form by entomologists interested in the Trombiculidae. *John W. D. Megaw.*

Greenberg, M., Pellitteri, O. J. & Jellison, W. L. **Rickettsialpox—a Newly Recognized Rickettsial Disease. III. Epidemiology.** *Amer. J. Pub. Health.* 1947, July, v. 37, No. 7, 860–68, 1 fig.

The authors describe the epidemiological conditions associated with the remarkable outbreak of rickettsialpox in the course of which the cause and mode of infection of this newly-discovered disease were detected [see this *Bulletin*, 1947, v. 44, 411, 707 and 897]. Between January and October 1946, 124 attacks occurred among about 2,000 persons living in a "housing development" consisting of three blocks of buildings, each of which was made up of 23 three-storied houses in which accommodation was provided at the rate of three or four rooms for each family. The affected locality was suburban in type, it was 15 miles away from the centre of New York City and was "surrounded at a distance by large lots of unkept grass, weeds and scrub forest."

A few cases occurred early in 1946, but they were not diagnosed or were regarded as aberrant chickenpox. The highest incidence was in July and August. Persons of all ages, of various occupations, and of both sexes, were equally affected; the incidence was strictly associated with residence in the houses of the area.

A thorough investigation was carried out by the New-York-City Department of Health between July and October with the results already stated in the previous papers, from which it appears that the disease is caused by a newly isolated rickettsia—*R. akari*—which is transmitted by a mite—*Allodermanyssus sanguineus*—whose host, a house-mouse—*Mus musculus*—is a natural reservoir of infection.

The vector mites were found on the walls of incinerators and of some rooms in the buildings, also on house-mice which infested the irregularly used incinerators and the buildings in general.

From 19 houses in which mites were found, 67 cases were reported, whereas from 41 houses in which no mites could be found there were 42 cases.

The patients rarely knew that they had been bitten; none of them had seen a mite or insect at the site of the initial lesion.

Since the completion of the investigation, 20 additional cases were seen by the authors in four of the five city boroughs: most, but not all, of these cases were in buildings with incinerators, which, if irregularly used, were found conducive to mouse and mite infestation. In every affected house mice were found. *John W. D. Megaw.*

YELLOW FEVER.

Durieux, C., Boiron, H. & Koerber, R. Sur l'existence d'un réservoir de virus amaril animal en Afrique. [**The Existence of an Animal Reservoir of Yellow Fever in Africa.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3 4, 111–18, 1 map.

During 1944, the authors examined the blood of 33 baboons, *Papio papio*, and one green Monkey, *Cercopithecus aethiops sabaeus*, aged about 1 to 3 years, and all caught in a small area at Medina, near the Gambia frontier. Twenty-nine baboons and the Green Monkey gave strongly positive immunity reactions against yellow fever, in other words the surprisingly high proportion of 88·2 per cent. of those examined. The results of the tests at Dakar during the past few years on 46 African monkeys, including 24 baboons, gave only one positive (a baboon from the French Sudan) and the results of other observers have never given proportions of infection reaching more than about 20 to 25 per cent.

The authors re-examined their sera with the use of the fractionating method, making separate tests with the serum-globulins and with the serum free from albumins. It was shown that the immune bodies were present in the serum-globulins, and that the positive results could not be explained by the presence of non-specific substances in the serum free from albumins.

It is evident that wild animals ensure the maintenance of yellow fever infection in certain parts of Africa and remain a permanent menace to neighbouring populations.

The authors advocate systematic vaccination as the simplest and most effective measure of preventing yellow fever outbreaks. *E. Hindle.*

HADDOW, A. J., SMITHBURN, K. C., MAHAFFY, A. F. & BUGHER, J. C. **Monkeys in relation to Yellow Fever in Bwamba County, Uganda.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 677–700, 5 figs. [15 refs.]

In a previous paper [this *Bulletin*, 1942, v. 39, 759], MAHAFFY *et al.* reported the isolation in 1941 of yellow fever virus from a human patient and from wild-caught mosquitoes, *Aëdes* (*Stegomyia*) *simpsoni* Theo in Bwamba County, Uganda. Yellow fever virus was again isolated from *A. simpsoni* in June 1942, and from forest-dwelling *Aëdes* (captured in uninhabited rain-forest) in April 1944. As it is known that over 90 per cent. of the entire population of Bwamba is still immune to yellow fever as a result of vaccination, these isolations imply the persistence of the disease among the wild animals of the Semliki forest in the County.

In a survey prior to the isolation of the virus from the mosquitoes, one of five red-tail monkeys (*Cercopithecus nictitans mpangae* Matschie) was found to be immune to yellow fever. Since that time, continuous studies have shown that of the many groups of animals investigated, yellow fever immunity exists among the monkeys only. One hundred and fifty (150) Bwamba monkeys were studied between March 1942 and November 1944, chiefly by examination of blood samples collected in the field, but over twenty live monkeys were also used for protection tests and experimental work.

Fourteen species and subspecies of Primates have been found by the authors in Bwamba. The species important in relation to yellow fever are the red-tail and the lowland colobus (*Colobus polykomos uellensis* Matschie). In juvenile and sub-adult age grades, immunity was low in all areas. Mosquito catches made in tree-tops in Bwamba have shown that the species chiefly suspected of being involved in the transmission of animal yellow fever in the forests are mainly arboreal. Consequently, it was at first thought that the more arboreal species of monkeys might show a higher incidence of immunity to yellow fever than those which spend much time on the ground, but it was found that the difference between the groups of partly terrestrial, mainly arboreal and arboreal monkeys was not signifcant. However, it still remains almost certain that transmission must occur mainly in the trees, for certain species which rarely descend to the ground show a very high incidence of immunity. It follows that the vector probably is most active at a time when all monkeys are in the trees, *i.e.* at night. Observation showed that all monkeys, including the partly terrestrial baboon, take up their sleeping posts about a quarter of an hour before dusk. Field and laboratory investigation suggest that *Aëdes africanus* Theobald may be the principal vector in this community.

It is suggested that the lowland colobus monkey is the main species involved in the monkey-to-monkey yellow fever cycle of the uninhabited forest areas, that the red-tail monkey plays an important part in bringing the virus into contact with man, and that the remaining species are of less importance in the local epidemiology.

The incidence of immunity increases with increasing age. In Bwamba, the susceptible monkey population becomes immunized at the rate of 27 per cent. per year. It is believed that yellow fever is truly endemic among the monkeys of the Bwamba lowlands. A small amount of evidence supported the theory that the offspring of immune mothers possess passive, congenitally-acquired immunity to yellow fever for a few months after birth. *F. O. MacCallum.*

ANDERSON, C. R. & ROCA-GARCIA, M. **The Reaction of Woolly Opossums (*Caluromys laniger*) to Yellow Fever Virus.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 161–76. [15 refs.]

In 1941, BUGHER and his colleagues [this *Bulletin*, 1941, v. 38, 434; 1944, v. 41, 475] found that marsupials of a number of different species were susceptible

to infection with yellow fever virus, and later suggested that marsupials may play an active rôle in the maintenance of jungle yellow fever. Most of the original studies were confined to *Didelphis marsupialis*, but later workers [*ibid.*, 1944, v. 41, 749] have used *Metachirus nudicaudatus* and *Metachirops opossum*.

The present authors have studied the effect of yellow fever virus on another species, the woolly opossum (*Caluromys laniger*). The animals studied were all trapped in regions of Colombia where yellow fever is endemic and where cases have been discovered within the past few years. Several different strains of yellow fever virus were used, but more than half the animals received a strain (*Chichimene*) isolated in a rhesus monkey infected by a bite of wild-caught *Haemagogus* mosquitoes.

Seventy-two (72) per cent. of the opossums were found to be susceptible to the virus on subcutaneous inoculation. None of the animals died of yellow fever, nor were any specific microscopic changes present in animals dying of other causes, but virus was detected in the blood stream for several days after inoculation in those animals classed as susceptible. The variation of susceptibility in relation to dosage of virus extends over a broad range.

Immunity in inoculated animals was determined by the results of reinoculation or estimation of neutralizing antibody in the serum by means of the intracerebral neutralization test in mice.

The majority of animals (94 per cent.) which had circulating virus later showed evidence of specific neutralizing antibody. Most of the animals developed detectable antibodies by the end of the second week, and the majority of animals actually showed their maximum response at this time, though in a few the maximum response did not occur till after 30 days. Following this response, some animals maintained their neutralizing antibody, but in others the antibody level began to decrease. There was no consistent relationship between the rate of disappearance of antibody and the intensity of the earlier response, or intensity of the infection. When the animals were reinoculated after the disappearance of antibody, circulating virus was found or neutralizing antibodies reappeared.

It was found that some animals which had circulated virus did not produce neutralizing antibodies. Also a number of animals that were immune to reinoculation had lost their once detectable antibodies. In others, in which circulating virus had not been detected, neutralizing antibody appeared; this discrepancy may have been due to the lack of sensitivity of the test for detecting minute amounts of virus. No animal with a positive neutralizing test just before inoculation circulated virus. *F. O. MacCallum.*

SNIJDERS, E. P., POLAK, M. F. & HOEKSTRA, J. **Jungle Yellow Fever in Surinam.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 861–8. [15 refs.]

This is a continuation of previous studies of yellow fever in Surinam reported by SCHÜFFNER and his colleagues in 1938 [this *Bulletin*, 1939, v. 36, 18, 25]. In the hinterland, the results showed that 26 per cent. of 78 men but only 4 per cent. of 48 women of the Bush-Negroes had yellow fever immune bodies in their blood. The women tend to stay in the villages and the men are foresters, but even so, the villages are situated in the middle of the forest and it is remarkable that the rate is so low among the women. It is suggested that the vector may be a night-biting mosquito.

Though the number of sera examined was small, a different result was found in testing the aboriginal Indians. Here the rates for men and women were practically the same (29 and 25 per cent. of 42 men and 16 women, respectively).

In the agricultural regions on the coast the plantations are situated near forest. Human infections are fairly common and probably of the jungle type. The capital, Paramaribo, is in close contact with the agricultural region and is visited yearly by many inhabitants of the jungle, but there are no indications that yellow fever prevailed here after 1909. However, penetration by the virus is possible and the authors recommend *Aëdes aegypti* control and mass vaccination. *F. O. MacCallum.*

British Guiana. **Yellow Fever Service. Medical Department. Annual Report 1946** [de Caires, P. F., Chief Officer]. 11 mimeographed pp., 1 map.

The Yellow Fever Service of British Guiana [see also this *Bulletin*, 1946, v. 43, 1136] ceased to exist as a separate organization at the end of 1946, becoming a part of the Mosquito Control Service from 1947 onwards. During 1946 very successful *Aëdes* eradication work was carried out in Georgetown and New Amsterdam, and in the Demerara River Estuary, Bartica and Mackenzie, all of which are now free from *Aëdes aegypti*. This satisfactory result is due in part to the routine measures previously described, in part to the use of DDT ; but the chief human factor was the high standard of efficiency maintained in the field staff of Inspectors. A bonus system for good work, and ruthless dismissal of incompetent persons, contributed to this end ; the author remarks that a single incompetent inspector may, and has, cost the Government thousands of dollars and much loss of time.

It is interesting to note that houses sprayed in 1945 with 5 per cent. DDT in kerosene, at Plaisance, remained free from *Aëdes* 17 months later, whereas these mosquitoes were constantly found in some 28 per cent. of control houses. Phenothiazine is an efficient larvicide in water containers, but does not control the breeding of *Culex* in pit latrines.

No case of yellow fever was reported in the Colony during 1946.

Charles Wilcocks.

Burruss, H. W. & Hargett, M. V. **Yellow Fever Vaccine Inactivation Studies.** *Pub. Health Rep.* Wash. 1947, June 27, v. 62, No. 26, 940–56, 1 chart. [21 refs.]

[In the early days of yellow fever vaccination, the blood of most of the individuals injected was tested for neutralizing antibodies a few weeks later. If antibodies were not present, a second dose of vaccine was given. When mass vaccination with the 17D attenuated strain of yellow fever virus was introduced, such tests became impracticable, but it was shown that if sufficient virus was given to each individual (500 mouse m.l.d.), at least 96 per cent. developed demonstrable antibody in their blood and it is probable that the remainder also had some immunity. It was found that the 17D strain of virus was somewhat more thermolabile than the original pantropic or neurotropic strains, but the exact behaviour of the 17D virus vaccine (serum free) at different temperatures was not known at the time it was required in large quantities. It was known, of course, that the virus survived better below +4°C. than at higher temperatures, and it was recommended that large batches of stock or seed vaccine should be kept at −5°C.]

The authors have been carrying out detailed studies of survival time, at different temperatures, of the 17D virus in dried stock chick-embryo water-base yellow fever vaccine, since 1942, which have provided valuable information for those who are involved in the production, distribution and use of this vaccine, both in temperate and tropical zones.

It was found that desiccation in a temperature of 20°C. to 25°C. ("room temperature") was cheaper and more convenient than, and practically as efficient as, at any other set of temperatures. Two hours' desiccation was ample thoroughly to dry ampoules containing 1 ml. of vaccine, and 6 hours' was sufficient for ampoules containing 5 ml. when the air around the ampoules was at 20°C. to 25°C. There was an average loss of 34 per cent. of active virus during desiccation at room temperature and 40 per cent. at −22°C. to +40°C.

Each of 20 desiccated vaccines held in storage at −9°C. to −32°C. for 3 years was still adequately potent for use at the end of that time. Vaccines stored at −5°C. to −7°C. and warmer showed considerable loss of active virus during a storage period of 2 years. For these reasons, it is recommended that desiccated vaccines be kept at −20°C. to −25°C. which can now be done at a reasonable cost.

Adequately desiccated vaccines may still be sufficiently potent for use after an exposure of several weeks to a tropical temperature. When several batches of vaccines were exposed at 37°C., an average of 90 per cent. of virus was lost in 2 weeks, and 99 per cent. in 8 weeks. A very small amount of active virus was present after 104 weeks. An interesting observation was that in each of 8 different lots of vaccines, there was an increase in titre after exposure for 7 or 8 hours at 25°C. to 37°C. An exposure of 8 hours at 100°C. and 7 hours at 110°C. was required to inactivate all virus.

A useful point for those concerned with inoculation of large groups of people was the finding that vaccine diluted 1 : 1 to 1 : 100 with saline remained adequately potent for 6–20 hours at 37°C. However, it is recommended that 1 : 1 and 1 : 10 suspensions be used within 1 hour of preparation and 1 : 100 suspensions within 10 minutes. *F. O. MacCallum.*

DENGUE AND ALLIED FEVERS.

WILBAR, C. L., Jr. **Control of Dengue in Hawaii.** *Amer. J. Pub. Health.* 1947, June, v. 37, No. 6, 663–74, 4 figs.

Dengue had not been known to occur in Hawaii since 1912, so that when the disease appeared in Honolulu in July 1943 it was feared that a great epidemic might occur and that the war effort might be seriously hampered. Accordingly, very elaborate measures of control were adopted; these at one period involved the employment of nearly 400 persons, who carried out the usual methods of mosquito destruction and the spraying of houses and their surroundings with pyrethrum and DDT insecticides.

In Honolulu there were 1,496 cases with three deaths among the population of about 250,000 persons. In the rest of Hawaii, with a similar population, there were only two cases.

The epidemic reached its peak in October 1943, and thereafter declined rapidly so that only sporadic cases occurred after mid-December 1943. After the middle of 1945 no further cases were reported.

The *Aëdes*-breeding index in Honolulu was reduced within two months from 5·7 per 100 houses in September 1943 to 1·0 per 100 and was then maintained at the lower level. [From the chart it appears that the index rose to 3·5 in early April 1944 without being followed by a recrudescence of the epidemic.] *John W. D. Megaw.*

DUPORT, Maria & TEODORESCU, Ana-Maria. Contribuţiuni la studiul phlebotomilor in România. [**A Study of *Phlebotomus papatasi* in Rumania.**] *Rev. Stiintelor Med.* Bucharest. 1946, Jan.–Apr., v. 35, Nos. 1/4, 46–55, 3 figs. French summary.

The authors report the appearance of *Phlebotomus papatasi* in relatively large numbers in Bucharest, more particularly in certain limited areas. During the year 1946, for the first time *Phlebotomus* carried by railway from the Constanza district have found favourable conditions for development in Bucharest.

The B-dul Basarab area, near the *Gare du Nord*, where these insects are established, had been heavily bombarded and there were a number of heaps of rubble which probably constituted larval breeding places. Furthermore, the unusual heat and dryness of the Mediterranean climate during the year were favourable to the survival of adult forms.

Sporadic cases of three-day fever occurred and were easily mistaken for other clinically similar febrile diseases. *H. J. O'D. Burke-Gaffney.*

ANDREEV, L. A. [**Contribution to the Question of Sandflies and Sandfly Fever in the Province of Alma-Ata.**] *Izv. kazakh. Fil. Akad. Nauk.* Alma-Ata. (Ser. zool.). 1943, No. 2, 30–33, 1 fig. [In Russian. English summary, p. 126.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1947, July, v. 35, Pt. 7, 111.]

Over 200 sandflies collected between 26th June and 12th August 1939 in houses in the town of Alma-Ata in south-eastern Kazakstan and in villages in adjoining foothills of the Alatau mountains were all identified as *Phlebotomus chinensis*, Newst. Three females kept in the insectary laid 23, 32 and 38 eggs, but none hatched. It is concluded from the numbers taken that adult sandflies are present in this region from mid-June to mid-August and most numerous in the first half of July. They attack man commonly, and probably not domestic animals, as they were not found in stables or cattle sheds. It is not known whether any disease transmitted by sandflies occurs in the area.

PLAGUE.

TOMICH, P. Q. **Preliminary Sylvatic Plague Studies in the Suez Canal Zone.** *J. Roy. Egyptian Med. Ass.* 1947, May, v. 30, No. 5, 239–46.

An attempt has been made by the author to investigate the existence of sylvatic plague in the Suez Canal Zone by examining rodents caught in villages and in the desert. In spite of the general opinion that plague in the Canal Zone is always imported, the author does not exclude the possibility that it may really be endemic, though very latent. Little or no evidence, however, has been found for this suggestion. A small strip of territory was selected for examination, with four villages on the Great Bitter Lake, of which Fayed village was the headquarters. The lake strip was separated from the desert by the Sweet Water Canal and rodents of the desert had little contact with domestic rodents.

Plague is recorded to have first appeared in Port Said in 1900 and there is only record of 90 cases in that city between 1900 and 1939. A first case of human plague appeared in Fayed during a Canal Zone epidemic in 1944, in which year there were 150 cases with 54 deaths. The whole Canal Zone was free again of plague by August 1946.

In this investigation, 119 rodents were examined for plague infection—56 domestic rats (*R. rattus* and *R. norvegicus*) and 62 desert gerbils and jerboas, with one *Mus musculus*. The fleas were mainly of the genera *Xenopsylla* and *Echidnophaga*. This is only a preliminary study of an important region and the conclusion so far reached is that " there is no evidence of plague infection at the present time among the various species of rodents collected."

W. F. Harvey.

Macchiavello, A. Reinfección pestosa de puertos peruanos por importación de sacos de yute provenientes de la India. [**Plague-Infected Fleas in Bales of Jute Bags imported into Peru from India.**] *Bol. Oficina Sanitaria Panamericana.* 1947, Mar., v. 26, No. 3, 225–8. [18 refs.] [English version 228–30.]

As long ago as 1934 Long and Mostajo [this *Bulletin*, 1935, v. 32, 448] put forward their conclusion that infected fleas could be the agency of direct introduction of plague into a country without even need for assuming that the presence of plague-infected rats was also a necessity. That opinion was opposed mainly on the ground that fasting fleas could not live longer than a month and that therefore a voyage lasting 80 days ruled out such a possibility. The present study brings support and proof for Long and Mostajo's explanation. That being so, it may be necessary to revise other explanations commonly adduced for the introduction of plague into South America, as for example that which occurred in 1904 when the steamer " Gladstone " with a cargo of jute bags brought plague to Antofagasta, Chile. During the present world war, jute bags were imported into South America in great quantity and with much less supervision over disinfestation than previously. Fleas of the genus *Xenopsylla* were found in bags in the course of importation into Peru. The bales had had no opportunity in transit for local contamination or infestation and no plague had existed locally for a number of years, while the fleas, all in a fasting condition, were taken from the interior of a bale ; some were found alive and some dead. A triturate of the fleas inoculated into a guineapig required four passages in series to produce attenuated plague, but the plague bacillus was isolated. Later still, under similar circumstances, another batch of fleas was collected, of which 8 *X. cheopis* were alive. " Six of these fleas were fed on one guinea pig which died of plague. The survivors of these fleas continued to feed on a second guineapig which also died of plague." The conclusion drawn is that positive evidence has been obtained of plague infection by fleas transported from India to Peru in bales of jute sacks. " The possibility that fleas arriving in jute bags might maintain their infection through a rat-flea cycle is discussed at length, and the probability of this mechanism is rejected." *W. F. Harvey.*

Indian Research Fund Association. Rep. Scient. Advisory Board for Year 1st Jan. to 31st Dec., 1946. 49–52. [**Plague.**]

The keeping qualities of plague vaccine are of great importance wherever it is used or manufactured on a large scale. Two main vaccines were investigated, casein hydrolysate and agar vaccine, at 0°C. and at 37°C. : the test applied was estimation of the size of the mouse protective dose, and neither vaccine showed great, if any, superiority over the other. The casein hydrolysate had an initial protective dose of 0·003 ml. and the agar vaccine 0·004 ml. A decided deterioration became manifest in both vaccines at the higher temperature. At 0°C. the dose was, for the former, still no higher than 0·0046 ml. and for the latter 0·0056 ml. after 20 months, but at 37°C. it had risen in the two cases to 0·014 and 0·015 ml. respectively.

Much is expected from the use of DDT in disinfestation, and yet it should not be used indiscriminately, for its action on fleas in natural rat burrows is dependent on adequate distribution and proper mixing with the burrow débris. In order to ensure this, the use of a " power duster such as is made by the application of a dusting mechanism to the exhaust pipe of a jeep will be very helpful and economical." On the whole it seems that cyanogas has advantages over DDT because it penetrates tortuous rat burows and kills both rats and rat fleas. *W. F. Harvey.*

CHOLERA.

PANJA, G. & GHOSH, S. K. **Isolation of Cholera Vibrios from Hooghly River Water at Calcutta.** *Indian J. Med. Res.* 1947, Jan., v. 35, No. 1, 1–2.

" Out of 524 samples of Hooghly river water 16 showed true *Vibrio cholerae* when examined by the candle-boric-peptone water method of Panja. Other methods tried were less satisfactory." [See this *Bulletin*, 1943, v. 40, 241.]

CHATTERJEE, H. N. **A Study of the Postmortem Bone Marrow from Cholera Cases.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 905–8, 5 figs. on 2 pls. [12 refs.]

This paper represents a continuation of studies reported by the author [this *Bulletin*, 1939, v. 36, 902], in which he described the pathological changes in the bone marrow in specimens from 25 cases of cholera. A further 15 cases constitute the material of the present study.

The characteristic microscopical finding was a great dilatation of the capillaries and of the sinusoids, which could be studied readily owing to the widening of the capillaries.

This capillary distension was seen in many other internal organs also ; but it was quite remarkable in the bone marrow, amounting in some cases to a dilatation in diameter of 15 to 20 times or more. It is suggested that the capillary changes may perhaps partially explain the extreme shock and collapse seen in cholera.

Leucoblastic reaction was constant, but variable ; eosinophiles in the marrow averaged 15 to 20 per cent. ; lymphatic nodules were found in a few cases.

Dilatation of the bone marrow capillaries is also found in epidemic dropsy, but the author distinguishes the bone marrow changes in that disease from those found in cholera on the grounds that in epidemic dropsy the general structure is oedematous, the capillary dilatation affects the sinusoids principally and there is no eosinophilia [presumably no increase in eosinophiles in the bone marrow ; the eosinophilia may be considerable].

The features described are illustrated by five photo-micrographs.

[The page number of the first reference in the authors' list should read 451, and not 51, as shown.] *H. J. O'D. Burke-Gaffney.*

INDIAN RESEARCH FUND ASSOCIATION. REP. SCIENT. ADVISORY BOARD FOR YEAR 1ST JAN. TO 31ST DEC., 1946, 1–4. [**Cholera.**]

This report relates both to studies projected, and to experiments which have not yet yielded satisfying results. Treatment of cholera proceeds on the lines of evaluation of sulphonamide drugs, and two sets of trials have been made, in the field and in Calcutta. If, rather arbitrarily, the several trials are combined,

it appears that : (1) In the field 35 patients were treated with sulphaguanidine and 36 with a placebo ; there were 6 deaths in the sulphaguanidine and 14 in the placebo series. (2) In Calcutta, out of 303 patients treated with sulphaguanidine (15 gm. daily) there were 10 deaths ; with sulphasuxadine (15 gm. daily) 7 deaths out of 190 ; with sulphadiazine (5 gm. daily) 2 deaths out of 99 ; and in the placebo series 8 deaths out of 292.

In laboratory examination of stools 320 cholera strains were isolated, 88·1 per cent. of Ogawa and 11·9 of Inaba subtype. It was found to be easy to prepare monospecific Ogawa " O " agglutinating serum, but difficulty was encountered in the case of Inaba because it showed considerable reduction of titre by absorption with Ogawa strains.

An interesting investigation is in progress to find whether the glucolipidic antigen fraction of LINTON and his co-workers, the " antigène glucolipidique " of the French school, and the " specific antigen " of WHITE, are identical or different. *W. F. Harvey.*

PANJA, G. & DAS, N. N. **Immunity after Intradermal Inoculation of Cholera Vaccine.** *Indian J. Med. Res.* 1947, Jan., v. 35, No. 1, 3–6.

" A preliminary study on the intradermal inoculation of cholera vaccine in human subjects was carried out with encouraging results and these have received support from certain observations on experimental animals. Further work is indicated."

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

WILLIAMS, T. H. **Intestinal Parasites in the Canadian Armed Forces.** *Canadian Med. Ass. J.* 1946, Mar., v. 54, No. 3, 249–52.

The author examined 500 returned Service men for intestinal parasites : all of the patients had been in the Mediterranean, Far East and other sub-tropical areas. Three specimens were tested in each case : examination was by direct smear and by zinc sulphate flotation when the former was negative ; motile specimens were stained by Quesnel's stain. Strict criteria were employed for the identification of protozoal species.

Entamoeba histolytica was found in 13 per cent. of patients, *E. coli* in 21·8, *E. nana* in 6, and *I. bütschlii* in 2 per cent. Of the flagellates, *Giardia intestinalis* accounted for 7·4 per cent. of findings. Helminths were less than 1 per cent., except *Trichuris trichiura* which amounted to 1·6 per cent. The low degree of helminth infection was surprising.

The author notes that a heavy *Giardia* infection was often the only finding in patients with recurring attacks of loose stools ; he is convinced that this flagellate is mildly pathogenic in certain cases ; the infection was usually cleared with mepacrine, 0·1 gm. three times daily for 5 days.

The author states that infection with *E. histolytica* was very high in persons returned from North Africa [the percentage was 28·57, but in fact this represents only 6 persons out of 21].

By means of three examinations on alternative days, *E. histolytica* was found in 60 per cent. of occasions on the first, 26 per cent. on the second, and 14 per cent. on the third examination.

As the infection is rare in Manitoba, the author, in co-operation with the R.C.A. and the R.C.A.F. obtained three specimens on alternate days from 100 members of the Forces who had enlisted recently and had not left Canada.

Only 2 per cent. showed *E. histolytica*. The figure for *E. coli* was 22 per cent., which was almost identical with that (21·8) found in those who had been abroad. Other amoebae accounted for 7 per cent. of findings. The author concludes from his experience and that of other workers that the incidence of pathogenic amoebae in Canada is about 1 per cent. [but the figures attributed to MILLER (this *Bulletin*, 1940, v. 37, 113) do not conform with those in Miller's paper].

A note of interest is the author's observation that " no procedure of examination of specimens for protozoa can equal the proficiency gained by experience in recognition of the various protozoa and cysts." He has repeatedly found protozoa in direct smears which were missed in flotation procedure [see also HILL, this *Bulletin*, 1947, v. 44, 901].

Patients were treated successfully for *E. histolytica* infection by means of emetine and carbarsone, or alternatively by diodoquin, which was less toxic.

H. J. O'D. Burke-Gaffney.

SCHENSNOVICH, V. B. & SMIRNOVA, E. N. [**Observations on the Discharge of Cysts of *Entamoeba histolytica*.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946 [1947], v. 15, No. 6, 82–7, 3 figs. [In Russian.]

It is a well-known fact that the discharge of active forms and cysts of *Entamoeba histolytica*, both in symptomless and clinical cases of amoebiasis, is subject to wide fluctuations, the exact nature and amplitude of which are still unknown. Since human carriers of the amoeba constitute the main reservoir of infection, it is important, from the epidemiological point of view, to study the dynamics of the discharge of cysts in such persons. With this object in view, the authors undertook prolonged observations on three carriers who have never shown symptoms of amoebiasis. Their stools were examined regularly every 2–3 days for 277 (case *K*), 133 (case *F*) and 24 days (case *C*).

The method was as follows : 0·1 cc. of faeces was suspended in 10 cc. of tap water to which was added 1 cc. of Lugol's iodine solution. A drop of the 1 per cent. faecal suspension was placed in a Fuchs-Rosenthal chamber and the number of cysts was counted at a magnification of × 400 over the whole ruled area. The mean of three successive counts was estimated for 1 cc. of the 1 per cent. suspension. The results of these observations are shown in a series of diagrams, from which it is seen that the number of cysts discharged at different times varied considerably, *viz.* from 0 to 60,000 in 1 cc. of 1 per cent. suspension, [*i.e.* 6 million cysts per gm. of faeces], the fluctuation being characterized by a sudden increase of the number of cysts followed by a sharp decrease in the course of two to three days. There were negative days, when no cysts could be detected in the stools even after concentration.

The output of cysts was also subject to individual variation. Cases *K* and *C* sometimes discharged enormous numbers of cysts, and continued to do so for long periods of time, but in 8 per cent. of tests no cysts were present, while in 23 per cent. of tests their number was very slight. In case *F* cysts were continuously present in large numbers (up to 4,000 per 1 cc. of 1 per cent. suspension) during the first 30 days of observation. This period was followed by 3½ months in the course of which cysts were either absent or very scanty, the number of negative days amounting to 56 per cent. of the tests. These investigations have shown that the discharge of cysts in carriers does not conform to any law, but appears to be irregular. It probably depends on some individual factors which stand in need of elucidation.

However, this study gives an idea of the relative merits of the usual methods of diagnosis employed in amoebiasis. It again emphasizes the unreliability of a single examination of faeces, for in some cases continuous examination of a

patient in the course of a month may fail to reveal an existing infection. Furthermore, the enormous numbers of cysts which are daily discharged by some carriers must be of the greatest epidemiological importance, especially under unsatisfactory sanitary conditions. On the other hand, the finding of scanty cysts in some carriers is not a justification for disregarding them as a source of dissemination of cysts. *C. A. Hoare.*

ROBERTS, Enid W. **The Part played by the Faeces and Vomit-Drop in the Transmission of** *Entamoeba histolytica* **by** *Musca domestica*. *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 129–42, 4 figs. [27 refs.]

The experiments described in this paper confirm previous work regarding the number and persistence of *Entamoeba histolytica* cysts in the faeces of flies (*Musca domestica*) having access to stools containing these organisms; the results also show that the cysts are deposited in the vomit drops, an aspect of the subject that has hitherto received little attention.

After reviewing the literature and describing her experimental technique, the author gives an account of the results of her experiments. These show that of 107 flies fed on a standard emulsion of *E. histolytica* cysts prepared from patients in hospital, 68 flies passed 147 faecal drops containing 1,792 cysts during 31 hours' observation. Cysts were noted in the fly faeces as early as five minutes after feeding and were recorded at all times during the period.

Of the same flies, 69 passed vomit-drops containing cysts. From 20 flies, 312 vomit drops were obtained during a period of nine hours; of these, 163 (52 per cent.) were negative, 100 (35 per cent.) contained one cyst, 27 (8 per cent.) contained two cysts, and the remainder three to eight cysts.

Observations were made on the fly's method of feeding on *E. histolytica* emulsion in three forms—as a liquid, as a thick, viscid film, and as a thick, completely dry film. In the first, the fluid was sucked up the opening between the labellae; each time the proboscis was removed from the food, a residue of débris which remained attached was dislodged and left on the slide; this residue was seen to contain a concentration of cysts. By the second method, more food was seen to enter by way of the pseudotracheae, the opening to the food canal being reduced. In the third method, the main food canal was almost completely closed and the food passed up the pseudotracheae.

To determine the size of the organisms which when fed to the fly may subsequently appear in the crop, and also the size of the organisms which may appear in the vomit drop, emulsions were prepared, one containing *E. histolytica* cysts (8 to 13 μ and 3 per field); a second containing *E. coli* cysts (12 to 20 μ and 8 per field) and a third containing oöcysts of *Eimeria acervulina* (22 to 25 μ and 25 per field). Twenty-four flies were fed, eight on each organism; five from each group were dissected immediately after feeding, and three from each group were kept alive for examination of the vomit drops.

The dissections showed that the crops of the five fed on *E. histolytica* contained cysts (4 per field); those fed on *E. coli* contained cysts (6 per field) and in the case of *Eimeria acervulina* the crops contained oöcysts (10 per field). These results suggest that particles larger than 12 μ tend to be filtered off on the way to the crop. Of the nine flies kept alive, the three fed on *E. histolytica* emulsion passed 57 vomit drops containing 30 cysts, those fed on *E. coli* passed 51 drops and only one cyst (12 μ in diameter), while no oöcysts of *Eimeria* were found in 47 vomit drops deposited by the three flies fed on this organism, thus suggesting that the majority of the *E. histolytica* cysts which enter the crop are held back by the pseudotracheae when the fly vomits.

The author suggests that the cysts which appear in the vomit drops are not derived from the crop but are those which have become wedged in the pseudotracheae and are later flushed out by fluid from the crop or from the salivary

glands. This is merely conjecture as the route has not been ascertained with certainty. *H. S. Leeson.*

PARVIS, D. Sull'accertamento diagnostico dell'amebiasi e su un metodo rapido di colorazione delle amebe intestinali. [**Diagnosis of *E. histolytica*; a Rapid Method of Staining Intestinal Amoebae.**] *Ann. d'Igiene.* 1942, Oct., v. 52, No. 10, 458–64. [11 refs.]

The only certain diagnosis of *E. histolytica* infection depends on finding the active amoeba or its cysts in the stools. Other laboratory methods of confirmation—cultivation, complement fixation, animal experiment, presence of Charcot-Leyden crystals—may prove negative, particularly in the case of carriers. The surest method is examination of the fresh stool; failing that, staining by Weigert's iron-haematoxylin has proved satisfactory in the author's experience. This is a modification of Heidenhain's method and results in much saving of time, for there is no need of a mordant.

The details are, briefly, these: Fixation in Schaudinn's fluid, 20 minutes (longer is immaterial; it does no harm); alcohol (70 per cent.) with Tr. iodi to a sherry colour, 20 min., alcohol (70 per cent.), 30 min., wash in water, 2 min., stain with Weigert's haematoxylin, 3 min., wash in running water, 5 min. (or more), dehydrate, clear and mount, 20 min. The whole process takes 1 hour 40 min., whereas Heidenhain's takes some 3–4 hours.

H. Harold Scott.

THERON, P. **Surgical Aspects of Amoebiasis.** *Brit. Med. J.* 1947, July 26, 123–6.

The mortality rate after operations on patients with untreated amoebic infections is considerable, owing to: (*a*) reduced resistance leading to increased liability to post-operative complications, hypoproteinaemia is frequent in amoebic infections; (*b*) interference with wound healing, leading sometimes to ulceration of the skin of the abdominal wall, especially after colostomy; (*c*) a tendency to breakdown of intestinal suture lines, leading to faecal fistula or general peritonitis; (*d*) the development of an acute amoebic dysentery, simulating severe bacillary dysentery during the immediate post-operative period; (*e*) occurrence of a mild hepatitis during the post-operative period. Every candidate for operation who has served in the tropics, whether he gives a history of dysentery or not, should have a stool examination and possibly a sigmoidoscopy.

Atypical acute hepatitis must be distinguished from acute cholecystitis, perforated peptic ulcer and appendicitis. Pain, tenderness and resistance may be so generalized as to suggest general peritonitis, and the signs may be maximal in the right iliac fossa. Occasionally, vomiting, constipation and distension may suggest acute intestinal obstruction. The clinical picture may change in one or two hours, so examinations should be repeated at short intervals. The lower thoracic region should be examined by palpation, gentle "fist" percussion and auscultation. In the presence of constipation a stool may be unobtainable, so sigmoidoscopy should be done in all doubtful cases. Moderate leucocytosis, with a polymorphonuclear count of only 75–80 per cent. is characteristic. Radiological screening may show the right cupola of the diaphragm elevated and fixed, if abscess formation has occurred. If doubt still exists and operation is not urgently indicated, a therapeutic trial of emetine will usually settle the diagnosis in 24–28 hours.

Hepatic abscess.—A history of dysentery is obtained in less than half the cases, and the dysentery may antedate the hepatic lesion by as much as 15 years. Although general debility, loss of appetite and progressive emaciation are

characteristic, many cases are recorded in which the diagnosis was established only after an apparently symptomless abscess had ruptured into the lung or general peritoneal cavity. Pyrexia is often inconstant or absent and adhesions may prevent downward enlargement of the liver. Leucocytosis is present in over 80 per cent. of cases, with the same type of differential count as is found in acute hepatitis. Screening should show immobility of the right cupola of the diaphragm, with obliteration of the costo-phrenic angle. A small sero-sanguineous effusion at the right lung base, with basal consolidation, is common. The general adoption of the emetine and aspiration treatment reduced the mortality from over 40 to 6 per cent., but open operation is still indicated in the presence of secondary pyogenic infection, where the abscess points on the abdominal wall or in an intercostal space, in cases where repeated aspiration has failed to cure, or when the abscess has ruptured into the peritoneal cavity. Closed drainage and local and parenteral penicillin are advised.

Perforation of a single ulcer of the colon usually leads to localized abscess. Four out of five of the author's cases recovered after simple incision and drainage. The friability of the colon renders treatment in the early stages difficult, and exteriorization, rather than closure by suture, is indicated.

Multiple perforations with general peritonitis may follow an acute attack superposed on chronic amoebic colitis, and it is usually stated that they are invariably fatal. The patient is very toxic, with a high temperature and severe diarrhoea, with *E. histolytica* in the stools, and does not respond to emetine or chemotherapy. Increasing tenderness over the caecum and pelvic colon are followed by accumulation of intraperitoneal fluid with little guarding or rigidity; finally there is sudden collapse. Post-mortem examinations on 15 cases showed an average of 5 perforations per case, with the caecum the commonest site; an important point noticed was a tendency by the omentum to seal off the perforations. The treatment advised is plasma transfusions, injections of 2 ml. of adrenal cortical extract at intervals of one hour, a small muscle-cutting incision and either a double-barrel ileostomy or a caecostomy with passage of a $\frac{3}{4}$ in. rubber tube into the ileum; post-operative treatment consists in intestinal decompression, intravenous fluid and sulphathiazole; emetine was not given for the first week. Seven of 15 patients operated on recovered; 12 not treated by operation all died.

Amoeboma. Fibrosis due to secondary infection may prevent a satisfactory response to emetine, and in such cases the diagnosis can only be made by microscopy after resection.

Acute typhlitis may present a clinical picture indistinguishable from that of acute appendicitis, and in spite of a careful history the element of doubt will necessitate laparotomy in some cases. Obstruction or interference with blood supply is the only indication for appendicectomy in the presence of active amoebiasis. To minimize the risk of faecal fistula, the stump of the appendix should be invaginated by a double purse-string suture of silk or linen, the suture line reinforced with omentum and a soft rubber drain placed in the paracolic gutter. Emetine should be administered immediately after operation.

Intestinal obstruction from inflammatory masses in the transverse colon was met with twice. One patient, a boy aged $3\frac{1}{2}$, died from bronchopneumonia following resection; the other, aged 54, recovered after exteriorization of the mass and drainage of the abscess.

Ileo-caecal intussusception due to inflammatory thickening of the colon may occur, and four such cases in adults are described. Two were fit for operation: in one case reduction was easy, in the other it could not be completely effected, so an ileo-transversostomy was made after sealing off the point of entry of the intussusception by suture; the devitalized portion of the intussusceptum was passed per rectum ten days later. Both patients recovered.

[Dunlop, writing of the treatment of severe cases of chronic dysentery amongst prisoners of war in Siam (this *Bulletin*, 1946, v. 43, 558), described 14 patients treated by ileostomy, of whom 3 died, 7 recovered completely and the others were improved.] *W. L. Harnett.*

Cluer, E. H. **Granular Proctitis treated with Succinyl-Sulphathiazole Suppositories.** *Lancet.* 1947, Aug. 2, 168–70.

Granular proctitis occurs as a late complication of, or concurrently with, dysentery affecting the lower bowel. It has to be differentiated from chronic bacillary dysentery, chronic intestinal amoebiasis, mucous colitis and low-grade chronic idiopathic ulcerative colitis. Three cases are reported of differing aetiology. The first resulted from chronic bacillary dysentery contracted, during the war, in Palestine ; the second resulted from amoebic dysentery contracted in Persia, and the third developed after haemorrhoidectomy, without any definite microbial infection.

Hitherto granular proctitis has proved most resistant to treatment, which is amply demonstrated by the multiplicity of therapeutic agents.

No reference has been found to the use of sulphonamide suppositories in British medical literature, though Howard (1945) in America has recorded the application of intrarectal powdered sulphonamides in non-specific recto-colitis. Sufficient time has not yet elapsed for an accurate estimate to be made of the value of the succinyl-sulphathiazole suppositories used in these patients, but the symptoms and signs were thereby greatly diminished and these preliminary results appear to indicate that this is by far the best and most economic method of applying sulphonamides to the diseased rectal mucosa. The suppository must necessarily come into intimate contact with it and can remain so for twenty-four hours. On the other hand, sulphonamide retention enemas can at best exert a temporary effect. Furthermore, the patient need not be kept in hospital after the diagnosis has been established.

In a note on the preparation of succinyl-sulphathiazole suppositories by R. H. Barclay, M.P.S., the recipe for each suppository is given as : Succinyl sulphathiazole, 3 gm., cocoa butter, 7 gm.

" The powdered succinyl sulphathiazole was placed in a warm dish, and half the quantity of melted cocoa butter was added. The two ingredients were stirred to form a smooth paste before the rest of the cocoa butter was added. When poured into the moulds and set, the finished product was a little over 2 in. long and $\frac{5}{8}$ in. in diameter."

Since there is no standard metal mould for such a suppository, glass tube moulds were made by removing the ends of test-tubes $\frac{5}{8}$ in. in diameter.

The suppositories are stored wrapped in " Cellophane ", and keep well at room temperature. *P. Manson-Bahr.*

Brelet, M. Note sur le pronostic de la dysenterie amibienne. [**The Prognosis of Amoebic Dysentery.**] *Rev. Paludisme et Méd. Trop.* 1947, June 15, v. 5, No. 37, 185–8.

The author modestly disclaims any deep scientfic *motif* in this study of amoebic dysentery. This is a simple account made in the special centre in Nantes for the purpose of assessing the pension of veteran soldiers with amoebic dysentery contracted in Syria and Morocco from 1916 to 1918.

The statistics concern 100 cases which can be taken as an index for assessing the whole. The author can positively assert that numerous sufferers from chronic amoebic dysentery recover completely. This point is not sufficiently emphasized in the many classical accounts of this disease during the last

thirty or forty years. The tendency to relapse is sufficiently emphasized but not the possibility of spontaneous recovery. Thus, out of the 100 test cases, no less than 44 terminated in complete recovery, which has been maintained.

Three dysenterics were operated upon for liver abscess and recovered entirely without further treatment, and it is suggested that the hepatic suppuration acted as a fixation abscess.

Out of the 56 who could still be assessed as ill, in only 15 has it been possible to verify the persistence of amoebae or cysts. The bowel disturbances of the remainder could be classified as enterocolitis.

As an example of the continued persistence of *E. histolytica*, the case of one pensioner is recorded in whom *E. histolytica* cysts were demonstrated in 1918 and who, though in good physical condition, continued to harbour them till 1932. Other cases recorded were less fortunate. Pulmonary tuberculosis complicated the picture in 9 dysenterics.

Several also were infected with malaria as well as with amoebic dysentery, but on later examination no stigmata of the former could be found. The conclusion is reached that malaria is more easily cured than dysentery.

P. Manson-Bahr.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Baltazard, M. Identification des spirochètes récurrents. Individualité de l'espèce *Spirochaeta recurrentis*. [**The Identification of Relapsing Fever Spirochaetes. The Individuality of the Species** *Spirochaeta recurrentis*.] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 77-81, 4 figs. on 2 pls.

The author finds that under dark ground illumination, *S. recurrentis* presents an appearance of uniform refraction which enables it to be distinguished from spirochaetes transmitted by ticks, which show a double contour [see this *Bulletin*, 1947, v. 44, 906].

Two photographs of *S. persica* and one of *S. gallinarum* are reproduced to show the appearance of tick-transmitted spirochaetes, and one of *S. recurrentis*, for comparison. [It is difficult to decide what interpretation to place on these appearances, although they do suggest some difference between the two kinds shown, possibly the result of variation in the diameter of the organisms.]

The well-known feeble pathogenicity of *S. recurrentis* in white mice has been partly overcome by the use of splenectomized mice, in which the infection is of longer duration. Out of 51 splenectomized mice inoculated with the spirochaete after various numbers of passages, 19 died or were killed at the end of infection ; of the 32 others, 2 had an infection of 2 days' duration, 11 of 3 days, 12 of 4 days, 5 of 5 days, and 1 of 6 days. Out of 21 normal mice inoculated as controls, 4 showed no spirochaetes in the blood, 4 an infection of 1 day, 6 of 2 days, 5 of 3 days, and 2 of 4 days. The number of organisms in the blood was about the same in both series, rarely more than 2 per field, and the true receptivity of the mice was not altered by splenectomy. Moreover, 18 passages in splenectomized mice did not have any effect on the virulence of the spirochaetes.

S. recurrentis is considered to be a very distinct form of relapsing fever spirochaete, cosmopolitan in distribution, distinguished by its epidemicity, method of multiplication in the human blood, its development in the louse, its failure to persist in *Ornithodorus*, its feeble or non-pathogenicity to small laboratory animals, and finally its uniform refraction under dark ground illumination.

E. Hindle.

PROVOST, C. & FLANDRIN, J. Trois nouveaux cas de fièvre récurrente hispano-africaine en Tunisie. (Complications neuro-oculaires.) [**Three New Cases of Relapsing Fever in Tunisia, with Neuro-Ocular Complications.**] *Rev. Méd. Nav.* (*Métropole et Outre-Mer*). Paris. 1947, v. 2, No. 2, 139–45.

KALFAYAN, B. H. *Leptospira icterohaemorrhagiae* **in Rats of Beirut.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 895–900.

The finding of two cases of Weil's disease in the hospital of the American University of Beirut led the author to survey the local incidence of leptospirosis in wild rats and to evaluate the best methods of examination, with special reference to possible kidney changes brought about by leptospirae.

Seventy wild rats were trapped in different places in Beirut between May 21st and October 8th, 1945; of these, 65 were *Rattus norvegicus* and 5 were *R. alexandrinus*.

Both kidneys were removed and one was divided into two, for silver-impregnation and for haematoxylin-eosin staining respectively. The other kidney was emulsified in saline, and the emulsion was examined under dark-field illumination: positive or suspicious specimens were cultured and inoculated into young guineapigs. The infected guineapigs either died in 5 to 10 days or were killed on the 10th day and examined at once, by methods similar to those employed in the case of the rats.

The silver impregnation method used was Nyka's modification of the Levaditi technique (*Ann. Inst. Pasteur*, 1934, v. 53, 243) and the cultures were made in Schüffner's buffered medium [see LEWIS, *Bulletin of Hygiene*, 1943, v. 18, 343].

Leptospirae were found in 7 of 20 rats above 20 cm. in length (35 per cent.) and in one of 50 rats under 20 cm. (2 per cent.). The author quotes many other workers in support of this evidence that the incidence of leptospirosis is appreciably higher in older rats.

In all of the 8 positive rats leptospirae were seen in the silver-impregnated kidney sections: no cases showed leptospirae by other methods but not in kidney sections, and it is evident that this technique gave the highest number of positive results. Next in order were dark-field examination of kidney emulsion (6 positive and one doubtful), guineapig inoculation (5 positive), and culture, which only revealed 4 positive cases.

In 8 rats *Trypanosoma lewisi* was found by dark-field illumination of kidney emulsions: seven of these rats were *R. norvegicus* and all of them were under 20 cm., confirming the belief that this infection is commoner in young rats.

In 3 rats the nematode *Trichosomoides crassicauda* was seen in sections of the kidney pelvis, in the form of a larva, a small adult male and a larger adult female, respectively; these were identified in haematoxylin-eosin preparations.

In the silver-impregnated sections, the leptospirae were found on the surface of the epithelial cells of the convoluted tubules, often in large masses easily detected and filling the lumen. The number of parasitized tubules varied from case to case and in different parts of the same kidney.

Haematoxylin-eosin sections of the 70 kidneys showed glomerulo-nephritis in 14 cases; this was seen only in the older rats (above 18 cm. in length). In six of these cases leptospirae were found.

Deposits of brown pigment, which appeared to be bilirubin, were found in cells of the convoluted tubules in 25 kidneys, but were abundant in only 11. Twenty-one of these occurred in older rats. The pigment was found in all of the 8 kidneys positive for leptospirae and was abundant in 7 of them. The pigment was present in the 14 nephritic kidneys and was abundant in 9 of them. The author considers it likely that the brown pigment was deposited in previously damaged cells.

The leptospirae could not be recognized individually by haematoxylin-eosin stain, but when they were abundant, the bluish mass which filled the lumen was distinctive. No histological difference was seen between the cells of the tubules infected with leptospirae and those which were not.

In conclusion, the author considers that demonstration of leptospirae in silver-impregnated kidney sections was the most reliable of the methods used in this survey. *H. J. O'D. Burke-Gaffney.*

PATTERSON, H. M. **Weil's Disease. Observations in Sixty-One Cases with special reference to the Use of Penicillin in Six Cases.** *J. Amer. Med. Ass.* 1947, July 26, v. 134, No. 13, 1077–80. [12 refs.]

The author previously gave a general report of observations in 37 cases of Weil's disease [see this *Bulletin*, 1945, v. 42, 42], and in the present paper discusses the management and treatment of this disease in a larger series of 61 cases.

Blood serum agglutination tests were performed on the 1st, 8th and 15th days after admission to the hospital. The tests were negative on the 1st day; usually showed no titre, or a low one, on the 8th day; and a high titre, or a rising one, on the 15th day. Nearly all the infections in Hawaii were found to be due to *L. icterohaemorrhagiae.*

A record of the patients shows that 44 received no special treatment, 7 sulphathiazole, 6 penicillin, 2 whole blood from donors who had recovered from Weil's disease, and 1 each with blood and either sulphathiazole or sulphadiazine. All the patients recovered, whether treated or not, and it is difficult to understand the author's statement that " the use of transfusions of whole blood from donors who have had Weil's disease should be the sheet anchor in the treatment of the severely ill patient ", based apparently on the clinical symptoms of these cases, all severe. The author's results support the view that sulphonamide compounds are not effective in this disease, but that treatment with penicillin is beneficial. *E. Hindle.*

YAWS.

FLOCH, H. & DE LAJUDIE, P. Traitement pratique du pian par la pénicilline en suspension dans de l'huile d'olive. [**Treatment of Yaws with Penicillin suspended in Olive Oil.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 1/2, 8–14.

The authors report four cases of secondary yaws (French Guiana) in whom clinical, but not serological, cure followed 100,000 Oxford units of sodium penicillin in sterile olive oil. The dosage was 1 ml. of oily suspension, containing between 10,000 and 15,000 units, daily for seven days. Its intramuscular administration was well tolerated. The activity of the suspension to *Staphylococcus aureus* was maintained after storage in an ice-chest for seven days. [See also DWINDELLE *et al.*, this *Bulletin*, 1946, v. 43, 1043.]

C. J. Hackett.

LEPROSY.

COCHRANE, R. G. **A Practical Textbook of Leprosy.**

This book is reviewed on p. 1026.

CHAUSSINAND, M. La transmission en série de la lèpre humaine aux animaux n'est pas réalisable par le procédé d'Ota. [**Failure to transmit Human Leprosy serially to Animals by Ota's Method.**] *Ann. Inst. Pasteur.* 1947, July, v. 73, No. 7, 682–4.

FITE, G. L., CAMBRE, P. J. & TURNER, M. H. **Procedure for demonstrating Lepra Bacilli in Paraffin Sections.** *Arch. Pathology.* 1947, June, v. 43, No. 6, 624–5.

The lesser "acid-fastness" of *Myco. leprae*, compared with *Myco. tuberculosis*, makes it difficult to stain appropriately in paraffin sections. FARACO (*Rev. Brasileira Leprologia*, 1938, v. 6, 177) showed that such material could be stained by oiling the sections and staining them with carbol fuchsin while they were in that state, but the present authors have found this method cumbersome, though effective.

They have obtained satisfactory results, irrespective of the techniques of fixation and embedding, with the following method, which, it is also stated, should do well with tubercle bacilli :—

1. Remove paraffin with two changes (1 to 2 minutes each) of a mixture of 1 part of oil (cottonseed, peanut or olive) in 2 parts of xylene.
2. Drain, wipe off excess oil, blot to opacity.
3. If mercury crystals are present, remove them with strong iodine solution (2 minutes), followed by hyposulphite or thiosulphate solution. Wash in tap water.
4. Stain cold for 15 to 30 minutes in any standard (but not concentrated) carbol fuchsin. Wash.
5. Decolorize with 1 per cent. concentrated HCl in 70 per cent. alcohol to a faint pink colour. One to 2 minutes will be required. Wash.
6. Counterstain with Loeffler's alkaline methylene blue for 30 seconds. Wash in tap water.
7. Blot, stand until dried out and mount in a synthetic mounting medium.

The oil hastens acid-fast staining and more regular staining results without the use of heat. The residual oil left in the sections after blotting prevents shrinkage and injury of the preparation : almost any oil will serve, though volatile oils are less useful. If a larger proportion of oil is added to the xylene, decolorization becomes more difficult.

The method "succeeds admirably with tissues indifferently fixed or embedded years previously where other procedures fail miserably."

H. J. O'D. Burke-Gaffney.

HELMINTHIASIS.

HSU, K. C. **A Survey of Human Intestinal Parasites in Chengtu.** *Chinese Med. J.* Shanghai. 1947, Mar.–Apr., v. 65, Nos. 3/4, 85–90. [18 refs.]

A number of workers have studied the incidence of intestinal parasites in Chengtu, in the Szechwan Province of China. The present author has studied the intensity of infestation in three groups of persons, namely (1) university

servants and their households (368 persons) ; (2) university freshmen students (337) ; (3) primary school children (471). He compared his findings with those previously reported by CHANG *et al.* [this *Bulletin*, 1941, v. 38, 375 ; 1943, v. 40, 851]. All specimens in the second and third groups were examined by fresh and stained smears and the number of eggs counted ; in the servant group, the number of eggs in each cc. of faeces was counted. The full results are given in a table ; five species of helminths and seven of protozoa were found.

Ascaris lumbricoides incidence was high among schoolchildren (85·3 per cent.) and relatively lower (46·8 per cent.) among freshmen ; in the servant group it was 68·7 per cent. Egg counts varied from 220 to 340,000, with a mean of 11,745 per cc.

Hookworm infestation was less than 1 per cent. in the schoolchildren and freshmen, but 17·3 per cent. in the servant group. Egg counts were from 200 to 19,600 with a mean of 2,106 per cc.

Trichuris trichiura was 2 per cent. in freshmen, 8·2 per cent. schoolchildren and 33·6 per cent. in the servant group.

Clonorchis sinensis was found in only 7 of the servant group and 2 of the freshmen. It is noted that raw fish is not ordinarily eaten in the province.

A single case of *Hymenolepis* infection in a schoolchild is believed to be the first recorded in the Province. No *Schistosoma japonicum* was found, though it is stated that previous workers had found more than ten cases in the neighbourhood of Chengtu.

Entamoeba histolytica accounted for only 1·7 per cent. of findings, being under 1 per cent. in the second and third groups, but it was 4 per cent. in servants. *E. coli* was also higher in servants, being 16·5 per cent. compared with 7·4 and 6·7 for schoolchildren and freshmen. Infestation generally was higher in servants, who suffered from as many as 4 or 5 species of parasites in some cases. *H. J. O'D. Burke-Gaffney.*

SCHWETZ, J. Note culicido-paludologique et malaco-schistosomique sur l'exploitation diamantifère de Bakwanga-Tshimanga (rivière Bushimaie). [**Malaria and Schistosomiasis [among Workers] in the Diamond Mines along the Bushimaie River.**] *Inst. Roy. Colonial Belge—Bull. des Séances.* 1947, v. 18, No. 1, 307–18, 1 map.

Bakwanga lies to the north and Tshimanga to the south of the Bushimaie Valley. The former is a post at which there are some 7,000 workers in the mines, well housed, and who with their wives and families amount to 15,000–20,000 inhabitants, distributed in camps at a perimeter of 5 kilometres round the European quarter. In this area are many craters of varied size, filled with water. Mosquitoes are fairly numerous ; more than four-fifths are *A. funestus*, 4·5 per cent. *A. gambiae* and 3 per cent. *A. nili*. The blood of 46 children under 10 years of age at one camp (Lomuele) was examined by thick drop and 34 of them showed malaria parasites, mostly *P. falciparum*, a few *P. malariae*, no *P. vivax*. Of 50 adult males examined in the same way 20 showed parasites, and of 49 adult women 17 were positive. In another camp, Kananga, one kilometre away from Bakwanga, no mosquitoes were found, but of 93 children below 10 years of age 61 were positive and of 72 adult women 22 were positive. At the time no men were examined as they were all away at work. Most of the parasites were *P. falciparum*, a few *P. malariae* and one *P. vivax*.

At Tshimanga all the author's time was taken up with bilharzia investigations, so he has nothing to say about malaria there, except that mosquitoes were numerous, mostly *A. funestus*, a few *A. gambiae*. The lie of the land, states the author, is not favourable to the use of DDT, apart from its cost ; the best ways of dealing with the menace are by pumping out the water and filling in the craters.

Schistosomiasis has increased much of late years. In 1932, among 3,000 workers, 80 (2·6 per cent.) were in hospital with the infection. In 1945, Dr. Sacré reported "22 per cent. of those with stomach complaints had bilharziasis" and 7·6 per cent. of all coming to the dispensary for treatment. At Tshimanga 14 per cent. of the workers were infected and 33 per cent. of dispensary patients had hookworms. In February 1946, the author and his assistants examined 39 men, 231 women and 47 children, 317 in all, in Tshimanga and found 4, 28 and 1 respectively, a total of 33, with bilharzia. In a brief stay at Bakwanga he found considerable numbers of *Planorbis adowensis* in a tributary of the Bushimaie, and at Tshimanga many *Bulinus* [*Pyrgophysa*] *forskali* in another tributary of the same river. *H. Harold Scott.*

CAWSTON, F. G. **Notes on Schistosomiasis from South Africa.** *J. Trop. Med. & Hyg,* 1947, Aug., v. 50, No. 8, 160–61.

MURRAY, A. J. Un nuevo caso de bilharziosis vesical en la República Argentina. [**A New Case of Urinary Bilharziasis in Argentina.**] *Rev. Asoc. Med, Argentina.* 1947, June 15, v. 61, No. 607, 411–13, 5 figs. [15 refs.] Summary in English by the author.

"A further case of bilharzial infection of the bladder is reported. The lesions were caused by Schistosoma haematobium. The patient had probably acquired the infection in Egypt.

"A biopsy revealed a characteristic granuloma formed round the parasite eggs."

MAKAR, N. **A Preliminary Note on Bilharzial Cancer of the Bladder.** *La Semaine de l'Egypte pour la Lutte contre le Cancer 23–30 Novembre 1938.* 89–112, 17 coloured pls. & 8 figs. [11 refs.] [1941. Cairo: Ministère de l'Hygiène Publique.]

Arguments in favour of regarding bilharziasis as a frequent cause of vesical cancer are well expressed by Dr. Makar, and though no actual proof of such an aetiological association has been produced, its probability seems well founded. Perhaps the most suggestive facts are: (*a*) Cancer of the bladder is the commonest form of malignant disease among the fellaheen of Egypt; and (*b*) most of this population are infected with bilharzia.

The chief part of Dr. Makar's paper is concerned with the surgical pathology and treatment of the disease, and his coloured illustrations of bilharzial lesions as seen through the cystoscope are excellent. A rather striking fact in his account of the age-incidence of vesical cancer in Egypt is that among 130 patients admitted with this disease to the Kasr-el-Ainy Hospital between January 1937 and October 1938, no fewer than 79 (60 per cent.) were under forty years of age. From the surgical standpoint, the only practical kind of prophylaxis consists of repeated cystoscopic examinations, once bilharziasis has been diagnosed, so that precancerous papillomata and ulcers can be properly treated at an early stage. *Harold Burrows.*

SCANDAR Bey, R. **Bilharzial Cancers in Alexandria.** *La Semaine de l'Egypte pour la Lutte contre le Cancer 23–30 Novembre 1938.* 295–300, 1 chart. [1941. Cairo: Ministère de l'Hygiène Publique.]

Like everyone else who has weighed the matter, Dr. Scandar is much concerned with the possible rôle of bilharzia as a carcinogenic agent. Among other facts bearing on the subject he gives the following laboratory findings:—

Site of cancer	Number of cases	Number showing bilharzial infection
Bladder	28	21
Prostate	3	2
Colon	35	2
Cervix uteri	28	1

The cancers of the bladder and prostate in which no bilharziasis was found, almost certainly, he says, were associated with such infection because the patients had been working in occupations in which this could not have been avoided. The author says that in some parts of Egypt as many as 90·5 per cent. of the general population have bilharzial infection of the urinary tract.

Harold Burrows.

ONSY Bey, A. **Rare Tumour Formations associated with Bilharzial Infections.** *La Semaine de l'Egypte pour la Lutte contre le Cancer 23–30 Novembre 1938.* 17–47, 44 figs. [1941. Cairo: Ministère de l'Hygiène Publique.]

After a short account of the life-history of the schistosomes and the method by which they enter the human body, Dr. Onsy gives a thoroughly detailed account of the histological changes which are produced in tissues in which eggs have been retained. These changes are illustrated by numerous micro-photographs. The great majority of the lesions occur in the pelvic organs where carcinomata and sarcomata are apt to be induced. Among the former Dr. Onsy includes cancers of the bladder, rectum, prostate, vagina, uterus and ovary; and the sarcomata mentioned originate in the bladder or intestine.

Of 5,665 malignant tumours examined in the Ministry of Health Laboratories, 365 (6·5 per cent.) were ascribed to bilharzial infection. These tumours "have been met with in such close association with chronic Bilharzia lesions, as to leave very little room for doubt of the existence of a causative relation between Bilharzia infection and tumour formation." *Harold Burrows.*

MAKAR, N. & FAWZY, R. M. **Bilharzial Carcinoma of the Urinary Bladder—a Note on some Unusual Cases.** *J. Roy. Egyptian Med. Ass.* 1947, May, v. 30, No. 5, 261–6, 6 figs. & 1 coloured pl.

Carcinoma of the bladder is stated to be the commonest form of cancer in Egyptian males, and is commonly fatal within two years. The relation of this condition to schistosomiasis has been the subject of much discussion and the author presents three unusual cases, in a schoolboy of 13, and two farmers of 42 and 40 years respectively.

In the first case, the patient had had repeated attacks of schistosomiasis. He was admitted with frequency of micturition and dysuria; a large ulcerating fungating tumour at the junction of the base and left lateral wall of the bladder was found at cystoscopy and it proved to be a squamous carcinoma with high cellular differentiation. A bilateral uretero-sigmoid anastomosis resulted in marked general improvement of the patient. This was made possible owing to the relatively sound condition of the ureters. The youth of the patient is noteworthy.

The second patient had symptoms of renal colic and frequency; cachexia and oedema of both limbs were present: schistosome ova were found in the urine. Rectal examination revealed the presence of a hard, stony mass proximal to an almost normal prostate: the mass was fixed and comprised the whole bladder base. X-ray examination of the lungs showed multiple opacities,

varying in size. This diffuse lung metastasis is a rare result : the complete absence of marked lymphatic secondaries supports the recent hypothesis that metastases of bladder carcinoma are carried mainly through the bloodstream along the paravertebral vessels. No treatment was regarded as being of value in this case.

The third patient had suffered severe suprapubic pain and persistent haematuria : he had had incomplete treatment for schistosomiasis. About two months earlier, soon after the pain had started, the patient noticed the gradual formation of a hard mass in the suprapubic region. Four weeks later, a pseudo-elephantiatic condition developed in the external genitals and upper part of both thighs. This indurated oedematous appearance was also seen in the skin, especially over the left groin : dark, hard, slightly tender nodules were scattered throughout the area. [All these features are illustrated in a colour plate.] There was bilateral enlargement, hardening and fixation of the inguinal glands. A small hard swelling was also seen at the lateral end of the left clavicle : this subsequently softened and showed slight pulsation and cracking ; X-rays showed a pathological fracture. Rectal examination detected a hard irregular mass in the whole bladder base ; microscopically one of the deep inguinal glands showed an undifferentiated squamous carcinoma with high mitotic figures. Spinal alcohol injections constituted the only treatment possible ; two of these, at a month's interval, caused much alleviation of pain and discomfort.

The special features of this case were the rapid onset of pathological sequelae ; the peculiar affection of the skin suggesting a cancer *en cuirasse*, which, the author states, has not hitherto been described in this condition, and the diffuse metastases.

The paper is illustrated by a colour plate, four X-ray pictures and 2 photomicrographs of biopsy specimens.

[While these unusual cases are of considerable interest, and this record of them is of great value, the claim made in the title has not been proved ; no evidence is given that schistosome ova or other specific changes were seen in the tumour tissues ; only one patient showed schistosome ova in the urine, and in the others, unequivocal signs of this disease are not recorded. In a country where bladder carcinoma and schistosomiasis alike are so prevalent, caution is needed, and something more than circumstantial evidence is required before the latter disease may properly be incriminated as a factor in the development of the former in a given case.] *H. J. O'D. Burke-Gaffney.*

BARTTER, F. C., COWIE, D. B., MOST, H., NESS, A. T. & FORBUSH, S. **The Fate of Radioactive Tartar Emetic administered to Human Subjects. I. Blood Concentration and Excretion following Single and Multiple Intravenous Injections.** *Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, 403–16, 2 graphs. [19 refs.]

The difficulties of estimating antimony in small amounts in tissue fluids has so far proved an obstacle to the study of the metabolic fate of drugs containing this element. This difficulty has, in part, been overcome in the present investigation by the use of radioactive isotopes of the metal in tartar emetic. This substance was prepared from Sb^{124} and Sb^{122} with half-life periods of 60 and 2·8 days respectively, obtained by bombarding the natural isotopes of the metal with deuterons in the cyclotron. Observations were made on 8 volunteers, seven of whom received single intravenous doses of the drug ranging from 0·253 to 1·6 mgm. Sb per kilo of body weight, given over a 5- to 10-minute period ; the last volunteer received a full therapeutic dose of 10·1 mgm. per kilo in 13 doses. Some of the usual toxic symptoms were experienced by the

patients. Excretion and blood concentration were measured by means of Geiger counters and scaling circuits, since the high energy gamma radiation aided detection in the presence of other organic material. In blood and urine, determinations were made mostly on dried specimens, while for faeces emulsions were used. The literature on the excretion of Sb after intravenous injection is cited. The present authors found that the blood level fell very rapidly and this probably accounts for the low efficiency of therapy by a single intravenous dose. At first there was a rapid elimination by urine and faeces, 80 per cent. being finally excreted by the former and 20 per cent. by the latter route. Experience with multiple injections suggests that it is possible to maintain a higher blood level by controlling the size and frequency of dosage. *J. D. Fulton.*

PESIGAN, T. P. **Results of a Brief Schistosomiasis Survey around Kake Mainit, Mindanao.** *J. Philippine Med. Ass.* 1947, Jan., v. 23, No. 1, 23–32, 3 pls. (1 map). [14 refs.]

Lake Mainit is near the northern tip of the island of Mindanao, Philippines, which itself is not far from the island of Leyte, where schistosomiasis was encountered during the recent war. The author gives a full account of two series of examinations of faeces of local inhabitants, in which 6 per cent. and 21·6 per cent. respectively of infections with *Schistosoma japonicum* were found. Many of the patients were apparently in good health.

The snail host, *Schistosomophora* (*Oncomelania*) *quadrasi*, was found in canals draining water from certain wells, and in rice fields. The sanitary habits of the people were poor, and other intestinal parasites were found in all faeces examined. *Charles Wilcocks.*

BONNE, C., BRAS, G. & LIE KIAN JOE. Echinostoma revolutum (Froelich 1802). Een nieuwe echinostoom van den mensch op Java. [*Echinostoma revolutum.* **A New Echinostome of Man in Java.**] *Med. Maandblad.* Batavia. 1947, June, No. 11, 207–9.

Four species of echinostome have been found in Indonesia infecting man: *Euparyphium ilocanum*, *Euparyphium malayanum*, *Euparyphium recurvatum* and *Echinostoma lindoense*. The new parasite, identified as *Echinostoma revolutum*, which is common in ducks and fowls and also in rats, was discovered in two adult Indonesians and a boy in Batavia during the Japanese occupation. Although this fluke closely resembles *Echinostoma lindoense*, also a known infection of fowls and ducks in Celebes, it differs from the latter by the greater length of its circumoral spines. The first intermediate hosts of *E. revolutum* are probably *Lymnaea rubiginosa* and *Anisus convexiusculus*. Second intermediate hosts could be *Viviparus javanicus*, *Pila conica* and other snails, which if eaten improperly cooked would be the source of human infection.
W. F. Harvey.

HARANT, H., GIROUX, J. & BRAUN-BLANQUET, Mireille. Petite épidémie familiale de toeniasis à *Hymenolepis*. [**A Small Outbreak of *Hymenolepis* Infection in a Family.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 89–90.

A child of 3½ was seen by the authors in Montpellier in January 1946. She had suffered from a refractory enterocolitis in August 1945, following a 3-weeks stay in the outskirts of Marseilles. Thereafter she passed a little blood in the stools almost daily. The stools numbered 4 to 6 each day, were sometimes " like

cowdung ", sometimes formed and glairy in the centre. There was an eosinophilia of 10 per cent. Examination of the stools showed many eggs of *Hymenolepis nana*.

The worms were expelled by the use of oil of *Chenopodium ambrosioides*, which plant was grown near Montpellier [the junior author will report later on the therapeutic action of this locally-extracted oil].

It was known that the village where the child had presumably been infected had been frequented by African troops from Senegal and Madagascar, and that during the summer 30 to 40 per cent. of the population suffered from persistent enterocolitis. Examination of the stools of 6 members of the patient's family revealed the presence of *H. nana* eggs in 3 of the children.

H. J. O'D. Burke-Gaffney.

DE MEIRA, M. T. V. & COITO, A. de M. F. Parasitismo por vermes intestinais em habitantes de uma povoação rural portuguesa. [**Parasitism by Intestinal Worms in the Inhabitants of a Portuguese Village.**] *An. Inst. Med. Trop.* Lisbon. 1946, Dec., v. 3, 277–91, 4 figs. [14 refs.] English summary.

" The authors present the results of their investigation on the parasitic infestation by intestinal worms in the inhabitants of a Portuguese village (Quiaios, Figueira da Foz).

" On 151 persons observed, 74 male and 77 female, between the ages of 2 and 22 years, all were infested as follows :—

10	persons by	*Ascaris lumbricoides*.
5	,,	*Trichocephalus dispar*.
131	,,	*Ascaris* and *Trichocephalus*.
3	,,	*Ascaris*, *Trichocephalus* and *Enterobius vermicularis*.
2	,,	*Ascaris*, *Trichocephalus* and *Hymenolepis nana*.

" The authors related this high infestation to the poor individual hygiene and point out the more convenient measures for the prevention of those helminthic infestations."

GALLIARD, H. Développement des microfilaires de *Filaria malayi* chez *Aëdes* (*S.*) *aegypti* et *Aëdes* (*S.*) *albopictus*. [**Development of Microfilaria of *Wuchereria malayi* in *Aëdes aegypti* and *Aëdes albopictus*.**] *C. R. Soc. Biol.* 1947, Feb., v. 141, Nos. 3/4, 105–6.

In a previous note [this *Bulletin*, 1939, v. 36, 150] it was established at Tonking that microfilariae of *Wuchereria bancrofti* can develop up to the infective stage in *Aëdes aegypti*. In 1942 this work was confirmed, but with *Aëdes albopictus* no success was obtained. In 1938 the author tried, without success, to infect both these species with the microfilariae of *W. malayi*, but in 1942 he succeeded, not only with *Aëdes aegypti*, but also with *Aëdes albopictus*. The patient on whom the mosquitoes were fed had no filarial symptoms, but 11 microfilariae were present in 10 cmm. of blood at 11.0 p.m. On the 10th day a larval filaria, completely developed, was found in the labium of *Aëdes albopictus*.

It is claimed that this is the first record of the development of any filarial species in *Aëdes albopictus* and the first record of the development of *W. malayi* in these two species of mosquito. The author asks what these results indicate. It seems at first sight that the number of mosquitoes employed is not proportional to the results. In the case of *W. bancrofti* no results were obtained with 90 specimens in one attempt and 70 in another. On the contrary, in two other instances he succeeded with 30 and 10 specimens respectively.

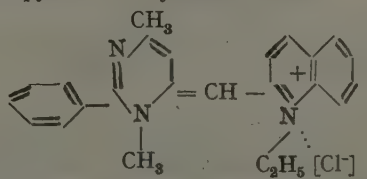
It may be argued that the percentage of mosquitoes infected may be proportional to the number of microfilariae in the peripheral blood, but this is not so, because he failed in one case with 80 microfilariae and succeeded, on another occasion, with 20–30 microfilariae per 10 cmm. of blood.

In 1938 the hypothesis was formulated which suggested that it might be a question of conditions favourable to the human carriers of microfilariae, but perhaps there might be in existence local races of parasites adaptable more or less to this or that vector. Recent researches in Samoa [Byrd *et al.*, this *Bulletin*, 1945, v. 42, 479], showed that *Aëdes aegypti* was refractory there, whereas in Porto Rico [Newton, Wright and Pratt, this *Bulletin*, 1946, v. 43, 52] in 5 per cent. of *Aëdes aegypti* experimentally fed complete development was observed. These facts would seem to support the latter idea.

P. Manson-Bahr.

Welch, A. D., Peters, L., Bueding, E., Valk, A., Jr. & Higashi, A. **A New Class of Antifilarial Compounds.** *Science.* 1947, May 9, 486–8.

Cotton rats infected with *Litomosoides carinii* [see this *Bulletin*, 1945, v. 42, 136] have been used as experimental animals in a search by the authors for a non-metallic drug effective in filariasis. Screening tests were made by giving maximum tolerated doses of drugs intraperitoneally, the doses being spaced in such a way that a favourable concentration was maintained in the tissue fluids during treatment. For this purpose 18 doses of drug were given at intervals of 8 hours. Forty hours after the last injection the animals were killed and filarial worms were removed aseptically from the pleural cavities and observed in sterile medium to determine whether death had occurred. *In vitro* studies were made with those drugs which proved active *in vivo*. Some members of the group of cyanine dyes were curative under these conditions. Experimental data suggested that oxidative enzymes were inhibited by the active substances and a characteristic grouping appeared necessary for activity. These substances also proved effective when given intravenously, but other routes of administration proved less satisfactory, and intramuscular or subcutaneous dosage caused tissue damage. The most active substance was 1′ethyl-3, 6-dimethyl-2-phenyl-4-pyrimido-2′-cyanine chloride,



and it almost invariably cured cotton rats when given in well-tolerated doses. In chronic toxicity tests in dogs and monkeys it was found that the drug was concentrated in the kidney, with accompanying mild damage to that organ. Recovery of excreted material indicated that the substance underwent change in the body. Treatment has now been given to 27 Porto Rican patients infected with *Wuchereria bancrofti*, in various dosages intravenously, and only mild toxic symptoms have been noted. The final results will be awaited with interest.

J. D. Fulton.

Ruiz Reyes, F. Estado actual del tratamiento de la oncocercosis. [**The Present Position in the Treatment of Onchocerciasis.**] *Medicina.* Mexico. 1947, June 10, v. 27, No. 533, 245–50. English summary.

The author states that surgical treatment is the treatment of choice in onchocerciasis, for which there is no specific curative drug. As an auxiliary to

surgical treatment, antimony has proved the most satisfactory drug. Details are given of 9 cases, in six of which anthiomaline was given following and additional to surgical treatment. *H. J. O'D. Burke-Gaffney.*

DEFICIENCY DISEASES.

WHITFIELD, R. G. S. **Anomalous Manifestations of Malnutrition in Japanese Prison Camps.** *Brit. Med. J.* 1947, Aug. 2, 164–8. [14 refs.]

In Japanese prison camps, malnutrition gave rise to a number of conditions which did not conform to the text-book descriptions of recognized deficiency states. Three such conditions are described in this paper.

"Painful feet" syndrome.—The clinical findings did not differ materially from those recently recorded by PAGE [this *Bulletin*, 1946, v. 43, 1060], CRUICKSHANK [*ibid.*, 1159] and GOPALAN [*ibid.*, 768] among others, and were consistent with Gopalan's identification of pantothenic acid as the causative deficiency. Vasomotor changes and gangrene were not observed : it is thought that these phenomena, very common in Page's series, were due to the prolonged immersion of the feet in ice-water, a practice from which the patients gained some relief of pain.

Cardiac beriberi.—Thirty cases of considerable severity occurred within 10 days. They were considered atypical in that neuritic lesions were slight and response to synthetic vitamin B_1 given orally in the form of "multivite" tablets, was slow.

Epileptiform fits.—Four men, within a period of a few weeks, had severe and prolonged tonic seizures. The cause remains unknown, but a smell of acetone in the breath of one suggested a sudden ketosis as a possible explanation.

Dean A. Smith.

SPRUE.

ANGULO, J. J. & SPIES, T. D. **The Determination of the Folic Acid Content of Foods usually consumed by Patients with Tropical Sprue.** *Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, 317–21. [10 refs.]

Following the successful treatment of certain anaemias with synthetic folic acid [SPIES *et al.*, this *Bulletin*, 1946, v. 43, 375] the authors made a study of cases of tropical sprue in Cuba and Porto Rico. In selecting the patients for study the following criteria had to be satisfied :—

1. Macrocytic hyperchromic anaemia.
2. Red blood count of 2·5 millions per cmm. or less.
3. Colour Index of 1·0 or more.
4. Megaloblastic arrest of sternal bone marrow.
5. Flat oral glucose tolerance test.
6. Free hydrochloric acid in gastric secretions after histamine stimulation.
7. "Fatty stools".
8. Weight loss.

The effectiveness of folic acid treatment was soon established. Attention was focussed early on the poor quality of the diet consumed by the patients with tropical sprue, which consisted mainly of bread, cornmeal, rice, starchy foods, coffee and sugar. When kept under observation on the usual diet, no improvement in their condition was noted, but a spectacular change occurred when folic

acid therapy was given in addition. The anaemia disappeared, there was gain in weight and well-being, and marked inprovement in the condition of the alimentary tract. The assay of folic acid in the raw edible portions of the above deficient diets following enzymatic hydrolysis was therefore undertaken, by means of the microbiological method of Teply & Elvehjem (*J. Biol. Chem.*, 1945, v. 157, 303) with *Lactobacillus casei* as the test organism. Yellow corn-meal, rice, coffee and other foods were found to contain little or no folic acid, and even yellow sweet potato, which had the highest content of folic acid contained only an insignificant amount. The above diets are deficient in certain other essential nutrients, as well as having a low folic acid content. While it has not yet been proved that a specific nutritional factor is lacking in sprue the experimental results lead the authors to state that—" These findings give added support to the hypothesis that tropical sprue is a nutritional deficiency disease." *J. D. Fulton.*

Howell, T. H. **Anaemia with Dyspepsia : a Syndrome encountered in Indian Troops.** *J. Trop. Med. & Hyg.* 1947, June, v. 50, No. 6, 110–12.

The condition reported was seen in about 60 Indian troops in Burma, most of whom had subsisted for some time on a diet of tinned milk, tinned vegetables, biscuits, jam and rice, in which the protein content was low, and was mainly of vegetable origin. Most of the men suffered from griping abdominal pain, excessive flatulence, anorexia, weakness, anaemia, and sore tongue, and most had recently had diarrhoea.

The anemia was hyperchromic in two-thirds of the patients, hypochromic in the others ; red cells counts varied from below 2,000,000 to 5,000,000, and haemoglobin from below 50 to 80 per cent. The aetiology of the condition is not clear, but the patients improved on a diet rich in milk, cheese, eggs and marmite, and after administration of iron and liver preparations.

The editor of the *Journal* (Dr. Napier) suggests that this condition may be para-sprue, as described in his *Principles and Practice of Tropical Medicine*, 1946. *Charles Wilcocks.*

VENOMS AND ANTIVENENES.

Grasset, E. & Goldstein, L. **Hyperglycaemic Action of Snake Venoms in relation to their Toxic and Antigenic Properties.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 771–88, 3 graphs.

Shircore, J. O. **An Account of Two Cases of Snake Bite treated with Injections of 2 cc. of 10% Magnesium Sulphate Solution.** *East African Med. J.* 1947, May, v. 24, No. 5, 200–201.

The treatment of snake-bite by the local application of solutions of magnesium sulphate has been known for many years. Wesley Cox mentioned it twenty years ago among first-aid measures after incisions [see this *Bulletin*, 1927, v. 24, 900], but in these cases the object in view seems to have been to increase serum secretion. In the two cases recorded by Dr. Shircore the action appears to have been more than this, in fact antidotal in character. In the first, a boy of 6 years bitten on the foot by a spitting cobra, *Sepedon haemachaetes*, the patient when seen 20 minutes later was restless, in much pain, with dyspnoea and cardiac distress and thready pulse. Within half an hour of the bite, 2 cc. of a solution of $MgSO_4$ [strength not stated, but in the second case 10 per cent. was used]. In 6–8 minutes the pulse improved

the restlessness diminished, and the local swelling disappeared by the fourth day. The second patient was an adult bitten on the foot by a puff-adder, *Bitis arietans*. When he was seen half an hour later he was much distressed, very restless, breathing with difficulty and with pulse barely perceptible. Two cc. of a 10 per cent. solution of $MgSO_4$ were injected through the punctures into the bitten area. Improvement set in in less than 10 minutes, the local swelling had much subsided in 24 hours and the patient left hospital, discharged fit, next day.

The author carried out some experiments with the venoms of these two snakes, using fowls. With the *Sepedon* venom the control died in one hour and 40 minutes; the other which received the salt 10 minutes after injection of the same dose of venom and at the same place, though at first drowsy and unable to eat or drink, gradually recovered and was well 10 days later. With the *Bitis* venom, 4 minims were injected into the pectoral muscle of a fowl, and this time 20 minutes were allowed to elapse before the salt was injected in the same place. The bird was incapacitated for 56 hours and then began to recover. There was none of the local sloughing usually seen in puff-adder bites.

H. Harold Scott.

DERMATOLOGY, AND FUNGUS DISEASES.

PANJA, D., DEY, N. C. & GHOSH, L. M. **Sporotrichosis of the Skin in India. (A New Species described.)** *Indian Med. Gaz.* 1947, Apr., v. 82, No. 4, 200–202.

"(*a*) A case of sporotrichosis of the skin in an Indian female vegetable dealer is described.

"(*b*) Literature on this subject is very scarce in India; this is probably the second authentic case reported from this country.

"(*c*) The species is pathogenic to common laboratory animals.

"(*d*) Detailed mycology shows that the colour of the growth resembles the European type species *S. beurmanni* but it differs from *S. beurmanni* in its biochemical reactions, morphology and some other points.

"(*e*) It differs from other known pathogenic species in many respects.

"(*f*) It is proposed to name this new species *Sporotrichum* (Rhinocladium) *tropicale* n. sp."

KERVRAN, P. & ARETAS, R. Deux cas d'histoplasmose observés au Soudan Français. [**Two Cases of Histoplasmosis in the French Sudan.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 1, 127–33. [11 refs.]

The first of the two cases was that of an African man 26 years of age who had a tumour the size of a hen's egg which appeared to be fixed to the right ascending ramus of the mandible. Two years before this, a wound had been inflicted on the gums during the operation of cleaning the teeth with a piece of wood, as is the native custom. As the tumour was fluctuating it was opened and about 20 cc. of yellowish pus were evacuated. In the pus, numerous yeast-like organisms measuring from 10 to 15μ in diameter and having thick capsules were found. After three weeks, during which iodide treatment was pressed, the patient appeared cured. Two months later, however, the abscess had re-formed. It was again opened and the pus, which contained the same organism, was removed. On this occasion two injections of 1 cc. of lipiodol were made into the abscess, which gave no further trouble.

The second case was in an emaciated African girl, 15 years of age, who presented herself for treatment on account of two tumours the size of oranges in the presternal region. A similar growth the size of a pea was found on the left side of the chest. In addition, there were excoriations covered with brownish crusts on the lower limbs and thorax, the lower limbs were oedematous and the abdomen distended with ascitic fluid. Examination revealed enlargement of the liver and spleen and a general adenitis. In pus extracted from the tumours and the excoriations the same yeast-like organisms as those found in the previous case were present in abundance. They were also found in liver puncture material and, after several failures, cultures were obtained from the blood on glucose agar. During the observations the child became comatose and died some hours later. At the post-mortem examination, ascites and glandular enlargement were noted. Both the liver and spleen were impregnated with yellowish nodules of various sizes, while an abscess occurred in the interior of the enlarged spleen. The inner surface of the skull showed patches of necrosis. The organisms were found in the spleen, liver, glands, bone marrow and necrotic areas of the bones of the skull. When cultivated, they developed after a few days a network of filaments with terminal spores which reproduced still further by budding. It is concluded that the organism corresponds to *Histoplasma capsulatum*, from which it differs, however, in its larger size.

C. M. Wenyon.

Santos Zetina, F. Un caso de erosion interdigital blastomicetica. [**A Case of Blastomycotic Interdigital Erosion.**] *Rev. Méd. Yucatán.* 1947, Apr. 30, v. 24, No. 4, 67–8, 1 fig.

Catanei, A. Du choix des animaux de laboratoire pour l'étude du pouvoir pathogène des champignons-parasites de l'homme. [**The Choice of Laboratory Animals suitable for studying the Pathogenicity of Fungus Infections of Man.**] *Arch. Inst. Pasteur d'Algérie.* 1947, June, v. 25, No. 2, 90–93.

The author discusses the laboratory animals most suitable for inoculation in testing the pathogenicity of fungi parasitic to man.

He describes the merits and defects of each one and the local and general effects commonly produced.

He concludes that while the guineapig is the most suitable animal for use in investigating the ringworm infections, the white mouse is particularly sensitive to other fungus infections; and for studying morphological characters *in vivo* this animal is to be preferred in the case of inoculation with the organisms of actinomycosis, sporotrichosis, mycetoma and histoplasmosis.

H. J. O'D. Burke-Gaffney.

GENERAL ENTOMOLOGY.

i. Pereira, M. de C. Culicídeos da provincia do Sul do Save (África Oriental Portuguesa). [**Culicines of the Province of Sul do Save, Portuguese East Africa.**] *An. Inst. Med. Trop.* Lisbon. 1946, Dec., v. 3, 341–64, 24 figs. on 13 pls. English summary (9 lines).

ii. ——. Culicini (Diptera, Nematocera) da colónia de Mocambique. [**Culicines of Mozambique.**] *Ibid.* 365–72, 1 fig. English summary (6 lines).

i. The author conducted a mosquito survey of the Province do Sul do Save in Portuguese East Africa during June to September 1944. In the first paper,

he gives a list of the places visited with the mosquitoes found in each. Twelve species and varieties of *Anopheles* were taken as well as more than forty culicines. Breeding places of some of the mosquitoes are illustrated by 24 photographs.

ii. The second paper is a list of the culicine species found on the above survey, together with their distribution and some notes on morphological characters where they differ from the type forms. *H. S. Leeson.*

Senevet, G. Le genre *Culex* en Afrique du Nord. I. Les larves. [**The Genus *Culex* in North Africa. I. The Larvae.**] *Arch. Inst. Pasteur d'Algérie.* 1947, June, v. 25, No. 2, 107–36, 4 pls. [35 refs.]

Colaço, A. T. F. **Study Trip to the Union of South Africa. Some *Culicoides* of the Transvaal.** *An. Inst. Med. Trop.* Lisbon. 1946, Dec., v. 3, 235–66, 12 figs. [Bibliography.] [Portuguese version 217–34.]

In this paper (which is in English) the author describes the females of *Culicoides habrius* and *C. hirtius* and the male of *C. milnei*; he gives a key for the identification of the Ethiopian *Culicoides* and an extensive, annotated bibliography concerning 86 species. *H. S. Leeson.*

Pavlov, P. Les tiques en Bulgarie et leurs hôtes vecteurs. [**Ticks and their Vectors in Bulgaria.**] *Bull. Soc. Path. Exot,* 1947, v 40, Nos. 3/4, 95–8.

This is a list of twenty-four species of ticks and their hosts as found in Bulgaria since 1935.

Delpy, L. P. Présence en Iran d'*Ornithodorus erraticus* (Lucas 1849). [**Presence of *Ornithodorus erraticus* in Iran.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 90–95, 1 text fig. & 7 figs. on 2 pls.

This is a full description of the tick, illustrated by photographs.

McCulloch, R. N. **The Adaptation of Military Scrub Typhus Mite Control to Civilian Needs.** *Med. J. Australia.* 1947, Apr. 12, v. 1, No. 15, 449–52, 2 figs.

The author reviews the work already done on the control of trombiculid mites or chiggers, and adds a concise account of the scrub-itch mites of Australia and experiments performed by him on ground disinfestation by gammexane. Australian and American workers are particularly concerned with control of scrub-itch, but their methods [see this *Bulletin*, 1946, v. 43, 1034] were inspired by war-time demands for the prevention of scrub-typhus, which is now known to be very widespread and is probably becoming increasingly established. Mites causing serious inconvenience to man are described from clay soils around Sydney ("grass-itch" *Acomatacarus australiensis* Hirst), along the S.E. coast ("titree-itch" *Trombicula samboni* Womersley), and in Queensland and New Guinea ("scrub-itch" *T. minor* Berlese and several other species), while *T. sarcina* Womersley in the Atherton highlands causes "black-soil itch" and a serious crippling of sheep.

In concert with antimalarial measures, chigger control is directed firstly towards personal protection by the treatment of clothing, and secondly against the mites on the surface of the soil. Personal protection by impregnating the clothes with phthalates or benzyl benzoate is generally applicable and can ensure 90 per cent. or more protection against scrub-typhus or scrub-itch. The treatment of the ground is applicable to important foci (*e.g.* infested gardens or

plantations) where man is frequently exposed : hitherto, this has been effected in scrub-typhus " islands " by clearing and spraying with crude oil, but the author has confirmed the remarkable efficacy of gammexane.

The standard treatment of clothing is the application of a teaspoonful of dimethyl-phthalate to a pair of socks, or an ounce to a set of socks, trousers and shirt, repeated after laundering. Dibutyl-phthalate will, however, last 3 boilings or 6 warm-water washes by hand. The author suggests applying DBP immediately before laundering to avoid the unpleasant collection of dust by the agent, and for home use recommends a shaker containing one part phthalate to 2 or 3 of water ; otherwise, hand-smearing or dipping in a 5 per cent. emulsion in 2 per cent. soap solution may be adopted. Benzyl benzoate, benzil and other agents are likely to replace phthalates in other theatres.

Experiments in a Sydney suburb showed that gammexane, hand-dusted on the soil [short grass, presumably] at the rate of 1–1½ lb. per acre of 14 per cent. crude benzene hexachloride in dust (=about 1·9 per cent. gammexane, and 1–1½ oz. of dust per 6 sq. yds.) gave an immediate reduction of over 95 per cent. in counts of larvae of *A. australiensis* Hirst, lasting for over a fortnight. The mite populations were estimated by counts on black cloth squares stretched on wire frames which were laid flat on the ground for 2–4 minutes, a method recommended by the author for relatively small populations.

[The effect on the nymphs and adults of the mites is most important and has not yet been studied. The author considers that two or three applications may suffice to suppress *A. australiensis* throughout a season, but the number of applications necessary will depend upon the life-cycle and habits of the mite, the effect on the adults, and the local conditions of application to the soil, so that proper methods will vary considerably with different mites and the terrain. Chiggers are generally most active in conditions of shade and raised humidity, and this has practical applications.] *J. R. Audy.*

LABORATORY PROCEDURES.

Bahrami, A. Un colorant de remplacement du Giemsa. [**A Substitute for Giemsa Stain.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 110–11.

When Giemsa stain was unobtainable, the author obtained good results with a " mercurial blue " and eosin.

To prepare the reagent, 1 gm. of $HgCl_2$ is dissolved in 150 cc. of distilled water : to the solution is added a sufficient quantity of 10 per cent. sodium hydroxide to obtain a precipitate of yellow oxide of mercury. This is removed and washed with several changes of distilled water until the fluid coming away is neutral to litmus paper. To the oxide of mercury 110 cc. of a 1 per cent. aqueous solution of methylene blue is added and the whole is kept in an autoclave at 120° for one hour. The liquid thus obtained is of a violet-blue colour : if it is too violet it should be rejected. The liquid is finally filtered and dried in a water bath.

To prepare the stain itself, 1 gm. of the powder and 0·5 gm. of eosin are dissolved in a mixture of 50 cc. of absolute methyl alcohol and 50 cc. of neutral glycerin. The mixture may be used after 24 hours. The stain is used in the same manner as Giemsa. *H. J. O'D. Burke-Gaffney.*

CASTELLANI, A. **The " Carbolic Acid Test " for the Detection of Quinine in the Urine.** *An. Inst. Med. Trop.* Lisbon. 1946, Dec., v. 3, 377–80. [Portuguese version 373–6.]

In this alternative to Tanret's test, 1·5 cc. of liquid carbolic acid is pipetted slowly along the wall of a test-tube containing 5 to 8 cc. of urine. A positive result is indicated by the appearance of a white disk at the surface of contact of the two fluids, within 3 minutes.

Another technique is to add 2 to 3 cc. of a 10 per cent. aqueous solution of carbolic acid to 5–8 cc. of urine : on shaking thoroughly, turbidity develops if quinine is present. As in the case of Tanret's test, a positive result also occurs if albumin is present : this may be distinguished from the presence of quinine by the fact that, in the latter case, the white disk disappears on gentle heating and re-appears on cooling ; in the case of albumin, it persists throughout.

Negative results were given with urines containing glucose, and with those of patients who had been taking sodium salicylate, aspirin, antipyrine and pyramidon. The urines of ten patients receiving quinine were tested by the new test and by Tanret's reagents. Both tests were equally sensitive and positive results appeared about two hours after quinine was taken and persisted for at least ten hours.

It is suggested that this test is simpler than Tanret's, since liquid carbolic acid is readily available in every hospital. *H. J. O'D. Burke-Gaffney.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

COOK ISLANDS, NEW ZEALAND. **Report of the Administration of the Government of the Cook Islands, including Niue, for the Year ended 31st March, 1947** [FRASER, P.]. 23 pp.

In 1946 the South Pacific Board of Health was established, with headquarters at Suva, Fiji, and the Cook Islands were brought within its scope. The staff of the medical department of the Cook Islands includes 2 European medical officers, and 7 Native medical practitioners.

In the year under review, general health was good. Outbreaks of poliomyelitis in Rarotonga, cerebrospinal fever in Atiu, and trachoma in other islands, which were mentioned the previous year, died down early in the year. Influenza became epidemic, and there was an outbreak of Bornholm disease (epidemic pleurodynia). Tuberculosis continues to be the main medical problem, and a new sanatorium is in full operation. Filariasis is prevalent on some islands.

The island of Niue is rather separate from the rest ; it is a coral atoll of 100 square miles, without natural fresh water. Its considerable population is served by one European medical officer and one Native medical practitioner, with their staffs. Yaws is prevalent, as are gonorrhoea, intestinal parasites, scabies and filariasis. There have been considerable numbers of cases of infectious jaundice [presumably epidemic hepatitis] and tropical myositis. In March 1947, there was an outbreak of bronchopneumonia, with 335 cases and 8 deaths, in just over 3 weeks. *Charles Wilcocks.*

AFRIQUE OCCIDENTALE FRANÇAISE. Rapport sur le fonctionnement technique de l'Institut Pasteur de l'Afrique Occidentale Française en 1945 [DURIEUX, C.]. [**Technical Report of the Pasteur Institute in French West Africa for 1945.**] 84 pp. 1947. Dakar : Grande Imprimerie Africaine.

This report contains a full and informative account of the Pasteur Institute in Dakar and its related services. Details are given of routine examinations made, together with notes on items of special interest. For example, it is noted that *S. haematobium* eggs were found 293 times (once in a European) in the course of clinical examinations of the urine : in addition, a systematic examination of garrison troops in Dakar, already made in 1943, was repeated in 1945 : *S. haematobium* eggs were found in 19 per cent. of 1,316 cases. The use of Pentamidine M. & B. in the treatment of schistosomiasis was studied in 15 Senegal troops : the average dose was 3 mgm./kgm. of body weight, in 1/20 or 1/30 solution in distilled water. The intramuscular route was employed, as undesirable reactions occurred in two cases where the drug was given intravenously. A total of 10 to 15 injections were given, the drug being injected once daily or on alternate days, and were well tolerated. Initial results were promising, but the apparent success was not maintained. Nevertheless, it is suggested that the results were sufficiently encouraging to merit further trials with another diamidine or the same one in larger doses or a different schedule.

Full details are given of histo-pathological examinations and comment is made on the predominance of carcinoma of the liver and epithelioma of the skin. Early diagnosis and treatment will be encouraged by the Cancer Treatment Centre now being established at Dakar.

The anti-rabies service produced a phenolized vaccine prepared by the Fermi method. In 1945, there were 35 treatments given by the Institute at Dakar, of which 11 were for Europeans : 24 courses were completed, with no deaths or untoward sequelae. An additional 290 courses were reported as having been given in the other 7 colonies in 1944, with one death, but no paralytic accidents. Information has since been received that 181 treatments were given in the French Sudan in 1944, with two deaths and with one death in an untreated person. Details are given of these treatments and the clinical features.

No change was made in the method of preparing yellow fever vaccine in Dakar : some 4½ million doses were issued in 1945. Despite difficulties in procuring and maintaining white mice, 1,058 protection tests were made, 1,040 of them with human serum. Of these, 617 were in connexion with comparative studies of the efficacy of the Dakar vaccine [this *Bulletin*, 1946, v. 43, 1135], 116 were concerned with the control of vaccination, 305 in the course of field studies and two in the diagnosis of yellow fever. The control of yellow fever vaccination by protection tests is discussed in relation to Dakar vaccine, used hypodermically and by scarification, and to vaccine obtained from other sources, such as 17 D and the Paris Pasteur Institute product. Epidemiological investigations included the examination of 250 blood specimens from the Gambia, of which 56·4 per cent. from four villages gave positive protection tests. Only one case of yellow fever was diagnosed in the Dakar Institute in 1945. This occurred in an unvaccinated European and diagnosis was confirmed by histo-pathological examination at autopsy.

A batch of 33 *Cynocephalus* monkeys captured in forest land in the Gambia showed 90 per cent. to be immune to yellow fever. Although no case of yellow fever had been reported in the Gambia for 7 years this finding, together with the high degree of human immunity reported above, indicated that there is recent evidence of the existence of the virus in that Colony. The significance of the nature of the immunity encountered in the different West African dependencies is discussed fully. Finally, this informative Report gives a full account

of 1945 experiments in the comparative evaluation of Dakar Yellow Fever vaccine, referred to above. *H. J. O'D. Burke-Gaffney.*

Congo Belge. Rapports sur l'Hygiène Publique au Congo Belge pendant les années 1940 à 1944 (condensés par le Service de l'Hygiène du Ministère des Colonies d'après les Rapports du Dr. van Hoof, Médecin en Chef de la Colonie). [**Belgian Congo : Reports on the Public Health during 1940-1944.**] 98 mimeographed pp.

This report of the Public Health in the Belgian Congo during the war years 1940–1944 embodies the annual reports of those years under one cover. It contains the vast amount of valuable factual information which one is accustomed to expect from the pen of Dr. van Hoof.

The report is largely statistical, with descriptive notes of some of the more prominent features, but its closely-filled foolscap pages of tables do not lend themselves readily to abstraction.

The first part of the report deals with general administration and infectious and other disease. Over half of the report is devoted to informative accounts of the medical facilities provided for the Africans, including the work of such organizations as "Foréami", the Congo Red Cross and other philanthropic and medical missionary bodies. Rural dispensaries and child welfare are described, and the various forms of medical instruction indicated. The report concludes with an account of hospitals, dispensaries, laboratories and hygienic measures, including industrial hygiene.

To those requiring detailed statistical information of medical administration and activities in the Belgian Congo during that period, this report will prove invaluable. *H. J. O'D. Burke-Gaffney.*

Gear, J. H. S. **The Geographical Distribution and Incidence of Disease in Southern Africa.** *Proc. Transvaal Mine Med. Officers' Ass.* 1947, Feb., v. 26, No. 290, 111–19. [26 refs.]

This lecture is a brief but lucid general survey of the communicable diseases of South Africa. The author divides his subject into a number of sections, dealing with factors which govern the geographical distribution of disease, and with the actual diseases, in their various groups. Much of the information is well known, but certain facts are particularly interesting. In spite of heavy rat infestation of the gold mines, leptospirosis has not been reported; although louse-borne typhus and tick-borne relapsing fever are common, louse-borne relapsing fever is not found. Positive yellow fever mouse-protection tests have been obtained with sera from the Zambesi valley and Ngamiland; the southern limit of the endemic area is much nearer to the Union than had previously been recognized.

All the diseases are preventable, and the author renews an old plea for the creation of an institute for the study of African diseases and the means of prevention. "Such an institute could make great contributions to the welfare of mankind." *Charles Wilcocks.*

Bolivia: Ministerio de Trabajo, Salubridad y Prevision Social. Servicio Especial de Profilaxia (Fundación Rockefeller). Informe Anual 1946. [**The Prophylactic Service of the Rockefeller Foundation in Cochabamba, Bolivia. Annual Report for 1946.**] 56 mimeographed pp., 14 maps. [1947.] Cochabamba.

[This excellent report of good work done is worthy of a better and more lasting set-up. A mimeographed record is liable to be pigeon-holed or set

aside and forgotten.] The main matters of interest dealt with in this report are: i. Yellow Fever; ii. Malaria; iii. Ankylostomiasis, and iv. The work of Health Units.

Yellow Fever.—At the end of 1945 and in the first two months of 1946 yellow fever broke out on the borders of Brazil and Bolivia, at Ascensión in the Canton of Petas, and invaded the provinces of Velasco and Chiquitos. The vector was not identified, but it is said that *Aëdes* does not exist and has not existed there. Altogether some 200 cases occurred and there were about 50 deaths. A team of workers was immediately despatched thither and a large part of the population was vaccinated. The last case diagnosed at the laboratory died on February 28th. Ten years had elapsed since this area had been visited by an outbreak of such dimensions.

Apart from this particular outbreak 16,055 were vaccinated in 86 localities in the Departments of Santa Cruz, La Paz and Tarija; many were re-vaccinated in zones where the infection was known to persist. Sixty-nine viscerotomy posts have been in action during the year and 491 specimens received; 19 of them were reported as positive. In an appendix, among other details are presented spot maps showing where outbreaks occurred during the year, where mosquito control was taken in hand, and tables noting the number of houses visited and the *Aëdes* index of each, the viscerotomy posts and the numbers of specimens sent from each of them in each quarter of the year.

Malaria.—Increase in endemicity was recorded in various parts of the country. At Aquile, near Mizque, there was an acute outbreak in which 80 per cent. of the inhabitants are said to have been attacked. Control followed the usual lines: canalization of streams, drainage, filling, the use of Paris green, of DDT, of petroleum, of larvivorous fish, etc. The chief vector is *A. pseudopunctipennis*, at times the only one found in the Valley of Cochabamba. Here the splenic index, which in 1943 among the schoolchildren was 14 per cent., was, in 1946, down to 1·3 per cent. and the parasite index fell from 2·5 to 0·1 per cent. In Misque the splenic index was 92 per cent. in 1942 and the parasite index 73; in the year under review these figures were 67 and 14 respectively. An addendum to this section gives the spleen and parasite indices of two dozen localities in different areas for each of the four years 1943–46.

Ankylostomiasis.—During the first half of the year, work was continued in the Trinidad area and later in San Ignacio de Moxos, Santa Cruz and Santa Ana. In the first-named, of 2,288 persons whose faeces were examined 1,840 (80·4 per cent.) were harbouring hookworm, 1,371 (59·5) showed ova of *Trichuris*, and 1,261 (55·1) those of *Ascaris*. 1,135 were treated, 832 with tetrachlorethylene and 303 with hexylresorcinol; nothing is said of the results obtained.

Health Units, two in number, in north and south Yungas La Paz, with bases at Coroico and Chulumani, do much good work in the treatment of yaws, vaccination against smallpox, faecal examinations for helminthic infection, especially ankylostomiasis, and in antimalaria measures.

H. Harold Scott.

BOOK REVIEW.

COCHRANE, R. G. [M.D., Ch.B. (Glas.), F.R.C.P. (Lond.), D.T.M. & H. (Eng.), etc.]. **A Practical Textbook of Leprosy.** With a Foreword by George R. McROBERTS, C.I.E., M.D., F.R.C.P., etc. pp. xi+283, 1 coloured pl., 174 figs., 6 diagrams, 2 maps, 1 chart & 1 plan. 1947. Geoffrey Cumberlege, Oxford University Press. London, New York & Toronto. [42*s.*]

In his preface the author states that: "It has been felt for a considerable time that a practical textbook on leprosy would fill a gap between the type of book which deals largely with the theoretical aspects of the subject and the smaller pamphlets." This is too modest a description of the present work, for it contains rather more pages, of a much larger size, than the third edition of "Leprosy" by ROGERS and MUIR, and consequently the text is actually half as long again as the earlier and more comprehensive work, but includes more illustrations. Moreover, the clinical and treatment sections of the earlier work by MUIR are of an eminently practical nature, while the present work includes much stimulating theorizing, all of which will not be accepted by other leprologists.

The history of leprosy is dismissed in two pages and the aetiology in four. Epidemiology occupies thirteen pages and is in accordance with modern views, except that state of civilization, climatic factors and predisposing causes are regarded as more subsidiary factors than others think. Age, contact with infective patients and type of disease are rightly emphasized as main factors in epidemiology, and Europeans and Mongolians are thought to be more susceptible than Africans and Indians. A short chapter on pathology brings out the modern view regarding the importance of WADE's opinion that the tuberculoid form shows good tissue resistance, with correspondingly good prognosis. It is well illustrated by microphotographs by the author. Diagnostic and serological tests are next dealt with and only the prognostic value of the lepromin is regarded as of importance. The Rubino test is not referred to and the author agrees with those who hold that lepromatous leprosy can produce positive Wassermann reactions in the absence of syphilis.

Having thus cleared the ground, the author goes on to the fullest sections of his work on clinical description and treatment. The signs and symptoms of leprosy are well described and illustrated by numerous photographs, which are good except for a few on diffuse lepromatous lesions which are difficult to interpret clearly. The Cairo classification is adopted, although it is recognized as requiring some amplification. Special attention is paid to the recognition of the earliest symptoms and this is one of the best parts of the work. The importance of differentiating between nerve cases of the tuberculoid form and the lepromatous types respectively is emphasized. Classification and the technique of examination are dealt with in a special chapter, and another is devoted to atypical lesions. The author regards these as rare and of an intermediate degree between the tuberculoid and lepromatous cases, but with a tendency to recover if the lepromin test is not negative. Pre-lepromatous maculae or incipient lesions of childhood are also described. Differential diagnosis from other diseases of the skin, including dermal leishmaniasis is well described and illustrated.

A chapter on reaction in leprosy is full and its different degrees are described. Interesting special chapters are devoted to lesions of the ear, nose, mouth and throat and of the eyes respectively, in which once more the author's great clinical experience enhances their value.

The next seven chapters, on treatment, cover 66 pages and constitute a valuable part of the work. In the opening chapter, some earlier methods of treatment are rightly dismissed briefly, and the great danger of inducing harmful reactions with iodides is emphasized. Sera, vaccines, aniline dyes and diphtheria formol toxoid are regarded as useless, and sulphonamides are only of local use in septic ulcers. Recent important work on the sulphones, such as promin and diasone is discussed, but their use is not advised until after further experimental trials: but it must be remembered that there is much delay in publication of a book at the present time. On the other hand, the modern method of injecting suitable preparations of chaulmoogra oils is relied on, although these preparations are not regarded as specific. The intradermal use of ethyl esters is preferred, and creosoted whole hydnocarpus oil advised for subcutaneous injections: details regarding their use are given. The treatment of different types of lesions is dealt with and also that of the all-important children. The control of reactions in leprosy is detailed and prescriptions are given. Special chapters are devoted to treatment of nerve, nose, throat and eye lesions, including operative measures which may be required. Another valuable chapter is devoted to the treatment of trophic ulcers, including operative measures, and one deals with complicating syphilis. Criteria of fitness for discharge, after-care and prognosis complete these sections.

The remaining 47 pages are devoted to the prevention and control of leprosy, based essentially on the author's long experience in Madras, where he has done much to forward their use. Unfortunately, in advocating the methods he has found to be of most use in Madras he has minimized the work of some of his predecessors and made some questionable statements. Thus, on p. 191 he attributes the change from indiscriminate segregation of all types of leprosy to selective segregation of only the infective cases mainly to the influence of the Manila Conference of 1931. Actually, its value was fully demonstrated in South Africa when Dr. Mitchell in 1923, on the basis of the reviewer's earlier writings on the subject, released one-third of the segregated patients after bacteriological examinations had proved them to be harmless, with resulting complete revolution of the old method of segregation and very favourable results, which are shown in a diagram in "Leprosy" (ROGERS and MUIR). Again, on page 193 he states that the British Empire Leprosy Relief Association was founded (1924) at a time when "it was thought that leprosy could be eradicated by treatment alone." In writing abstracts of leprosy papers for the last 25 years, the reviewer cannot recall any authority advocating treatment alone, for at a Leprosy Conference early in 1920 in Calcutta the reviewer, when advocating dispensaries for the treatment of early uninfective cases, also advocated as an essential complementary measure the founding in every province of India of agricultural colonies for the segregation of all highly infective nodular (now called lepromatous) cases Unfortunately lack of funds prevented that measure being adopted, except partially in comparatively rich Madras. Further, a medical memorandum by the reviewer which formed the basis of B.E.L.R.A. policy, strongly emphasized the same view. MUIR's "Propaganda, Treatment and Survey Method" which has been of immense value in disclosing the incidence of, and stimulating interest in, leprosy, is also lightly dismissed. However, the preventive sections of this work are worthy of close study, they emphasize the importance of child leprosy and village isolation of infective cases (advocated earlier by MUIR). This is of importance, because the segregation of any appreciable number of infective cases may be ruled out in India for lack of the huge funds required for that purpose.

Appendices deal with public health legislation, detailed descriptions of three sample surveys, and diagrams for recording the distribution and treatment of lesions. The bibliography contains over 120 references.

The scope of this work can be gathered from the above description. Its main value lies in its clinical and treatment sections. The fact that it appears under the auspices of the Oxford Medical Publications ensures it being well produced, but at a cost that makes it by far the most expensive British modern work on leprosy. Dr. Cochrane has done leprologists a service by recording in a convenient form the results of his long research and clinical experience of this difficult disease. *Leonard Rogers.*

It is with deep regret that we record the death on November 4th of Dr. W. H. KAUNTZE, *C.M.G.*, F.R.C.P., Chief Medical Adviser to the Secretary of State for the Colonies, and Chairman of the Honorary Managing Committee of the Bureau from 1945 to the date of his death.

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The fees for the whole course amount to 1000 Portuguese Escudos (approximately £10).

The Secretary will be glad to assist students in finding suitable accommodations in private houses, boarding houses and hotels in the vicinity of the School.

For further particulars write to the Secretary of the Instituto de Medicina Tropical, Travessa do Porto Franco Lisboa — Portugal.

NAPT

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